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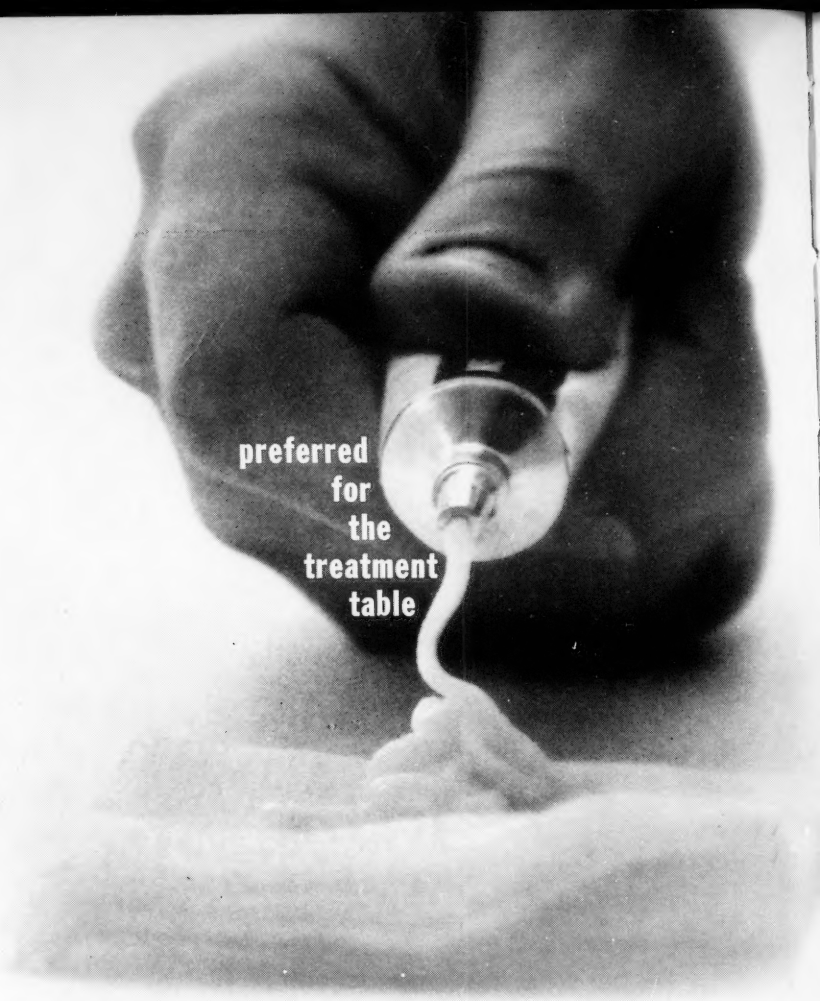

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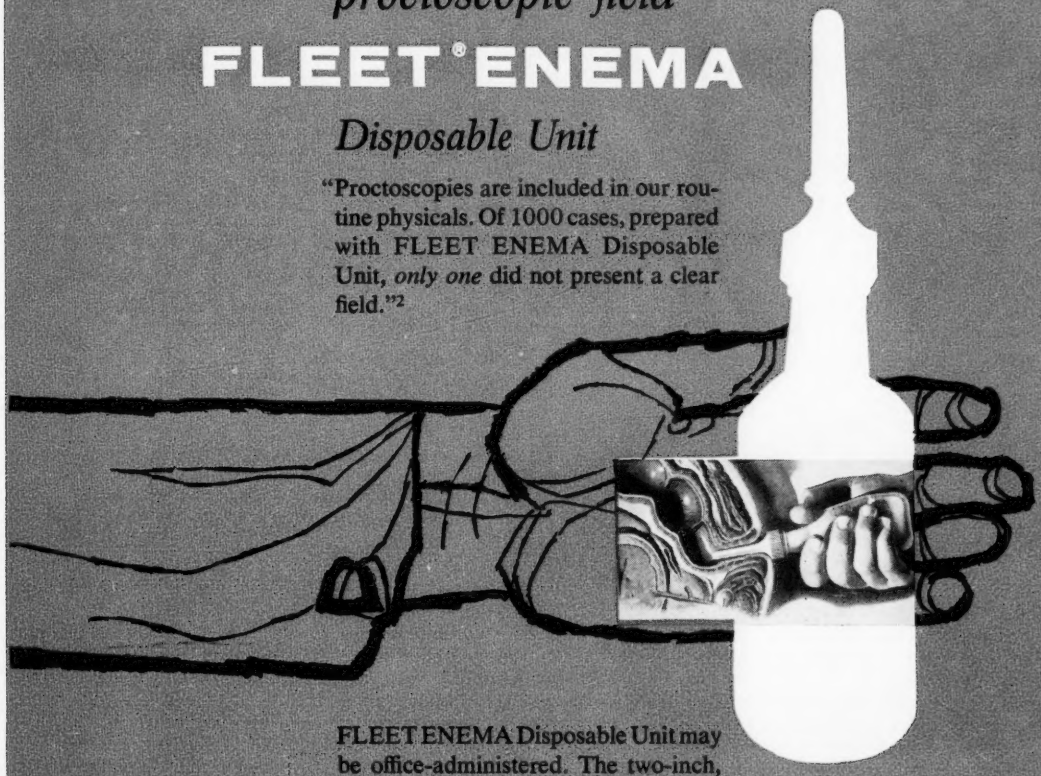

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The Industrial Medical Association was organized in 1915 as the American Association of Industrial Physicians and Surgeons. Its first annual meeting was held the following year. In 1951 the present name was adopted.

The purposes of the organization as stated in the certificate of incorporation (not-for-profit) are:

"The object of this Association will be to foster the study and discussion of the problems peculiar to industrial medicine and surgery; to develop methods adapted to the conservation of health among workers in the industries; to promote a more general understanding of the purposes of the medical care for employees; and to unite into one organization members of the medical profession specializing in industrial medicine and surgery for their mutual advancement in the practice of their profession."

Presently, the membership totals nearly 4000 physicians in the United States, Canada, Latin America, and other parts of the world. Physicians "who have an interest in Industrial Medicine" may apply for membership; specialization in this field is not essential. Regionally, the Industrial Medical Association has 14 Component Societies in the United States and one in Hawaii. Most Association members carry their membership through one of the component groups.

The Journal of Occupational Medicine, owned and published by the Industrial Medical Association, is sent monthly to each member as one of the advantages of membership.

The annual business meeting and convention is held in the spring. Since 1945, the convention has been held concurrently with the meetings of four other organizations having related interests—American Industrial Hygiene Association, American Conference of Governmental Industrial Hygienists, American Association of Industrial Nurses, Inc., American Association of Industrial Dentists. This combined meeting is known as the Industrial Health Conference.

The Occupational Health Institute, Inc., is a nonprofit educational organization created by the Industrial Medical Association to promote the cause of health in industry. Since 1951, the Occupational Health Institute has conducted the program of evaluation, approval and certification of Medical Services in Industry, on the basis of standards established by the Standards Committee of the Industrial Medical Association. This program was conducted by the American College of Surgeons for many years until its transfer to the Association.

The Association's headquarters office serves as a focal point for the Association's activities, and through its coordination of information regarding industrial health problems encountered throughout the country, it offers invaluable assistance to members on a host of specific subjects.

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Through its District Counselors, the Industrial Medical Association is represented regionally throughout the United States and Canada. Each district is served by a Counselor appointed by the President of the Association. The District Counselor reflects the attitude of the membership of his district in his relations with the national organization, and in turn, reports and interprets policies of the Association to the membership and the general public in his district.

An important function of the District Counselor is to serve in a liaison capacity with the Component Society of the Industrial Medical Association in his area. The District Counselor also is concerned with regional trends in industrial medical practice and in legislation bearing upon medical service in industry. He is ready to assist any physician with questions or problems.

In promoting the cause of industrial medicine, many District Counselors work with the industrial health committees of their state medical societies, they participate in teaching programs at hospitals or medical schools, and serve as speakers at meetings of groups that express interest in occupational health. Throughout these activities, the District Counselor attempts to stimulate membership in the Industrial Medical Association by acquainting others with the organization's purposes and facilities.

By keeping in close contact with members in his area, the District Counselor gains a familiarity with their work which enables him to make recommendations to the Association's officers and committees regarding those qualified for various positions or honors. He recommends members for committee work, and for fellowship, and recommends fellows for consideration for elective offices in the Association. He also recommends possible recipients for the awards presented at the annual meeting of the Association—the Knudsen Award, the Health Achievement in Industry Award, the Meritorious Service Award and the Merit in Authorship Award.

Many District Counselors also serve as Regional Consultants for the Occupational Health Institute, the educational affiliate of the IMA.

Journal of Occupational Medicine

The Diagnosis and Management of Accidental Radiation Injury

George E. Thoma Jr., M.D., St. Louis, and Niel Wald, M.D., Pittsburgh

ALTHOUGH the nuclear age had its birth almost 20 years ago, widespread utilization of nuclear reactors and of large quantities of radioactive materials beyond the confines of governmental facilities has undergone great acceleration only within the past five years. The liberalized Atomic Energy Act of 1954, with its emphasis on peacetime uses of atomic energy, helped to stimulate this development. Thus, the population potentially exposed to peacetime accidental radiation injury has also been expanded to include not only Atomic Energy Commission contractors' employees but also workers in private industry, as well as the general population in their vicinity. This, in turn, means that not only the AEC's industrial physicians, but physicians in general must anticipate the possibility of being obligated to deal with the clinical aspects of radiation injury with very small, but, nevertheless, gradually increasing frequency as the nuclear age advances. And in the disastrous event that the world's peacemakers fail in their tasks, the frequency of such injury may well mount uncontrollably. It is therefore of immediate importance that all physicians be familiar with the diagnosis and management of clinical radiation injury.

Present knowledge of the effects of known doses of various radiations on normal humans is mainly indirect. It comes from controlled experiments with mice, rats, rabbits, and monkeys in the radiobiological laboratory, from analyses of findings in therapeutically irradiated sick humans, and from retrospective studies of accidental human radiation exposures.

Several drawbacks are evident in these data. Because of the variations in radiosensitivity of different tissues in different species, the controlled laboratory studies are not readily extrapolated to man. The biological responses of recipients of therapeutic irradiation are not necessarily those of normal humans. In accidental exposures of normal humans, detailed precise measurements of dose and uniform selection of test parameters and procedures have not always been possible. Because of these drawbacks, it is deemed essential that certain medical guidelines be established for the management of cases of radiation overexposure, not only to facilitate the management of accidental clinical radiation injury in the individual patient, but also to expedite the accumulation of more useful data concerning such injury, as a basis for further improvement in its diagnosis and therapy.

To make maximum use of past experiences with radiation accidents in developing the guidelines for their future clinical management, all presently available data concerning human exposure from criticality accidents have been reviewed. Only normal case material in which the radiation exposure was acute, external, penetrating, and generalized has been con-

Dr. Thoma is with the Department of Medicine, St. Louis University School of Medicine. Dr. Wald is with the Department of Occupational Health, University of Pittsburgh Graduate School of Public Health. Work performed by authors as consultants to the Health Physics Division, Oak Ridge National Laboratory.

sidered. The clinical syndromes resulting from various protracted, internal, superficial, and localized exposures are too varied for the present purposes.

The sequence of events and resulting personnel exposures of each accident are reviewed and discussed in Part I, "Analysis of Past Accidents—Physical Aspects." Following a discussion of the clinical manifestations of radiation injury, the symptomatology and laboratory findings of the victims of these accidents are reviewed and analyzed in Part II, "Analysis of Past Accidents—Clinical Aspects."

Certain recommendations for diagnosis and management, based on the material reviewed, are made in Part III, "Recommended Medical Procedures." Despite their somewhat empirical and arbitrary nature, it is felt that their incorporation among the procedures used in dealing with these accidents will help to accomplish two vital objectives. These are, first, good immediate care of the patient at hand and, second, more effective therapy for future patients as a result of the improved compilation of usable long-term data concerning the deleterious effects of radiation in man.

Part I. Analysis of Past Accidents —Physical Aspects

Since the onset of widespread research and production activities in nuclear technology dating back to the inception of the Manhattan Project, there have been seven major criticality accidents involving significant overexposures of personnel to ionizing radiation (Table I).

In order to provide a better understanding of the nature and magnitude of these accidents, to demonstrate the problems of patient care, and to emphasize the need for the accumulation of long-term data of a standardized nature, each of these accidents is reviewed in chronologic order.

In addition to accident reports, a number of authors have summarized accidents and incidents involving radiation in nuclear technology activities, either as summary reports or as background or information material in the consideration of general or specific human radiation effects. Hayes[1] summarized accidents and incidents from June, 1945, through December, 1955, and extended the period to December, 1956, in a supplementary report.[2] Gerstner[3] included a summary of accidents up to 1955 as a part of his very comprehensive analysis and discussion of the acute radiation syndrome in man. Similar reports of other authors appear in the literature.[4-9]

TABLE I—CHRONOLOGY OF RADIATION ACCIDENTS

Accident	Date	Type
Los Alamos I	Aug. 21, 1945	Criticality (experimental assembly)
Los Alamos II	May 21, 1946	Criticality (experimental assembly)
Argonne	June 2, 1952	Criticality (reactor)
U.S.S.R.	1953-1954?	Criticality (reactor)
Oak Ridge	June 16, 1958	Criticality (processing)
Yugoslavia	Oct. 15, 1958	Criticality (reactor)
Los Alamos III	Dec. 30, 1958	Criticality (processing)

Accident Dosimetry

The characteristics of fissionable material vary with the mass and shape of the material. It is said to be "critical" when it is of such configuration that a nuclear reaction can be sustained at a fixed level of intensity. If the critical dimensions are exceeded, an exponentially increasing chain reaction will occur. Accidental excursions of this type produce variable intensities of fast neutrons and gamma rays. Accidents of this nature are referred to as criticality accidents. It is noted in Table I that all of these accidents were of this type.

Since the time of the first of these accidents (14 years ago), there has been a continuous evolution and improvement in the techniques and concepts of radiation dosimetry. For example, dose units such as the gram-roentgen are no longer believed to be significant indices of radiation exposure, and time has served to accentuate the complexity of the RBE concept. In a previous report,[10] an effort was made to reevaluate the dose assigned to certain individuals involved in nuclear accidents, using modern techniques of radiation dosimetry.

To put the physical dosimetry of past accidents on a common objective basis, the dose to a given individual is specified in terms of the absorbed dose (in rad), which would have been received by a small mass of tissue located at the position of the individual. This dose will be referred to as the first collision dose. It is realized that correlations of biological data with a single dose reading will be far from perfect unless other physical conditions of exposure are specified. Thus, as much information as is available on parameters such as radiation energy and angular distribution was considered in the previous report.[10]

The use of the rem dose unit is avoided entirely in this report, except as it appears in Table II under reported dose. First collision doses will be given in terms of rads to soft tissue for neutrons and gamma rays separately. This procedure is consistent with the desirability of establishing RBE factors for acute irradiation of man from accident data.

The method which has been found most reliable for evaluating the neutron dose to persons exposed in mixed radiation fields is the measurement of the amount of radioactive sodium (Na^{24}) which is produced when the neutrons interact with normal sodium (Na^{23}) in the body. It has been found that the neutron dose to the body may be related in a simple way to the spectrum of incident neutrons as determined from threshold detector measurements. This method of dose measurement might be termed "spectral" dosimetry and is described in detail in the previously mentioned report.[10] Likewise, the Na^{24} activation engendered in the body is very simply related to threshold detector measurements of the neutron spectrum. Hence, if one can estimate or measure the neutron spectrum escaping from a critical assembly, the Na^{24} activation in a man may be interpreted in terms of the first collision dose at his position. This method has been used below, whenever data on spectral distribution of neutrons are available. Estimates of the gamma-to-neutron dose ratio are used to allow one to assign both gamma and neutron doses on the basis of Na^{24} activation in the body.

TABLE II—SUMMARY OF EXPOSURE DATA

Accident	No. of Patients	Pt. Code* R	Pt. Code* L	Reported Total Body Dose Neutron	Reported Total Body Dose Gamma	Reported Total Body Dose Total	Calculated Total Body Dose Neutron	Calculated Total Body Dose Gamma	Calculated Total Body Dose Total
LASL-I	2	LA1	1	480 (rem)‡	110 (rem)	590 (rem)	297 (rad)	?	297+ (rad)
		LA2	2	31	0.14	31	18.2	2	20.2
LASL-II	8§	LA3	3	1930 (rem)‡	114 (rem)	2044 (rem)	1230	120	1350
		LA4	4	390	26.4	416	220	22	242
		LA6	6	186	10.7	196	120	12	142
		LA7	7	140	8.7	148	50	5	55
		LA8	8	55	4.37	59	33	3	36
		LA9	9	42	2.72	44	25	2.5?	27.5?
		LA10	10	33	2.41	35	20	2	22
Argonne	4	A1	1	14.2 (rep)	145 (rep)	189 (rem)¶	14.2	145	159
		A2	2	9.6	116	146	9.6	116	126
		A3	3	5.5	55	71	5.5	55	60.5
		A4	4	0.8	10	12	0.8	10	10.8
U.S.S.R.	2	R1	Kh	?	?	450 (r)	?	?	450
		R2	M	?	?	300	?	?	300
Oak Ridge	8	OR1	A	96 (rad)	269 (rad)	365 (rad)	96	269	365
		OR2	C	89	250	339	89	250	339
		OR3	D	86	241	327	86	241	327
		OR4	B	71	199	270	71	199	270
		OR5	E	62	174	236	62	174	236
		OR6	F	18	50.5	68.5	18	50.5	68.5
		OR7	G	18	50.5	68.5	18	50.5	68.5
		OR8	H	6	16.8	22.8	6	16.8	22.8
Yugoslavia	6	Y1	V	210 (rem)	630 (rem)	840 (rem)	320	320	640
		Y2	D	256	768	1024	250	250	500**
		Y3	M	214	642	856	290	290	580
		Y4	G	230	690	920	300	300	600
		Y5	H	174	522	696	210	210	420
		Y6	B	102	306	408	175	175	350
LASL-III	2	LA11				12,000 (rem)‡	2300	6900	9200
		LA12				135			

* First column (R) designates code used in this report. Second column (L) designates patient code that appears in the literature.

† Recalculation based on serum Na^{24} data, except Argonne and Oak Ridge cases.[13, 14, 16]

‡ The rem value expressed in the LA I and II cases are based on an assumed RBE value of 5 for fast neutrons with an approximate depth dose penetration equivalent to that of 80KV unfiltered X-rays.

§ Data on patient LA5 not available.

¶ Based on an assumed RBE value of 3 for fast neutrons.

|| Expressed in original report[15] in r only with no mention of neutron or gamma components. Total rad doses are assumptions only.

** Female patient whose weight is not available in the literature and might be considerably less than 70 Kg standard man, the value used in calculating this dose.

‡ Estimate ± 50%.

Dose estimates are made only for cases which satisfy the radiation exposure criteria established for this sudy, i. e., acute, external, penetrating, and generalized. Doses due to alpha and beta radiation, either internal or external to the body, are thought to be relatively unimportant, and are not considered.

Los Alamos Accident, LASL I

The first nuclear accident occurred at the Los Alamos Scientific Laboratory, Los Alamos, N. Mex., on Aug. 21, 1945. The clinical, laboratory, and dosimetry aspects of this accident were reported in detail by Hempelmann, Lisco, and Hoffman.[11] In a criticality experiment involving a metal system, a nuclear excursion occurred and two persons were exposed to the mixed radiation field from this assembly. One of them (Case LA1), who died after the accident, was touching the assembly when the chain reaction occurred and so received a very high dose to his hands and a smaller dose to the bulk of his torso. He was exposed to considerable gamma radiation from fission products after the reaction took place, while dismantling the experiment, and would possibly have survived had he left the room immediately instead. His actions during this period are not well known, and the total dose received is correspondingly uncertain. Neither he nor the other person exposed were wearing film badges at the time of the accident. Since the number of fissions which occurred in the assembly is not known accurately, the best index of his neutron exposure is the Na^{24} activity level in his blood. The neutron dose calculated from these data is 297 rad. The gamma first collision dose is impossible to ascertain owing to the uncertainty of his whereabouts in the immediate postcriticality period. Therefore his dose is given simply as 297 + rad in Table II.

Case LA2 was exposed at a greater distance from the reactor than was case LA1 and did not remain in the vicinity after the excursion. From measurements of the ratio of gamma dose to neutron dose leaking from the Godiva reactor[12] designed to reproduce as closely as possible the conditions of their accidents, it is estimated that the gamma-neutron dose ratio was approximately 1:10 in the LASL I accident, independent of distance from the reactor in this range of distances. The resulting estimate of his dose is 18.2 rad of neutrons and 2 rad of gamma.

Los Alamos Accident, LASL II

The circumstances surrounding the second major radiation accident at Los Alamos, on May 21, 1946, were quite similar to those in the first accident. Personal film badge data were not available, and data from badges located on the walls of the room were not very helpful. Eight persons were exposed to significant doses in this incident. It is felt that none of these victims received uniform total body exposures because of various amounts of partial body shielding. One fatality occurred.

The neutron doses to the exposed persons have been estimated as in the case of the LASL I accident, i.e., by using neutron spectral data obtained from the Godiva reactor, together with Na^{24} activation data from the blood of the patients. Table II shows the doses derived on this basis. It has been assumed that the gamma-to-neutron dose ratio was 1:10 for all those exposed. This is probably a good assumption, except for case LA9, who returned to the scene of the accident twice after his initial exposure. The previously mentioned report by Hempelmann et al.[11] also includes this second Los Alamos accident.

Argonne Accident

A reactor criticality accident occurred at the Argonne National Laboratory, near Chicago, on June 2, 1952. Four persons were exposed to a mixed field of radiation in which the gamma–neutron dose ratio was about 10:1. The pertinent clinical and dosimetric aspects of this accident were reported by Hasterlik and Marinelli.[13] There were no fatalities.

Patients 1, 2, and 3 were wearing film badges which were so blackened that it was necessary to evaluate the doses in terms of the reduced silver left after the development of the film. The gamma dose to Patient 4 was evaluated from a knowledge of his position and times of exposure to prompt and delayed fission gamma rays.

The gamma dose is given by the ANL group[14] in terms of first collision dose, i.e., the correction for the effect of the body on the dose received by it has been made. The doses were found to be fairly constant over the bodies of those exposed and can be considered as uniform whole body irradiation.

Threshold detector measurements of the neutron spectrum escaping from this assembly are not available. However, Hasterlik and Marinelli quote accurate neutron dose values determined with proportional counter dosimeters. These were obtained by measuring the ratio of fast neutron dose to gamma dose during the experimental run of the reconstructed reactor and applying this ratio to the film badge readings.

The resulting dose determinations, ranging from 159 to 10.8 total rad, are given in Table II.

Russian Accident

At some undisclosed time, presumably prior to 1954, a reactor accident occurred in the U.S.S.R., resulting in the "short general external" exposure of two persons to neutrons and gamma rays. The clinical course of the patients is detailed by Guskova and Baisogolov.[15] They assign doses of 300 r and 450 r to them but do not give the gamma-neutron ratio in the radiation field. No information is available concerning the structure and composition of the reactor, and so it is not possible to estimate this ratio. In addition, the methods of dosimetry used are not described. The dose assignments must therefore be regarded as ambiguous.

Oak Ridge Accident

A criticality accident occurred on June 16, 1958, in the Y-12 Plant at Oak Ridge, Tenn. Criticality was reached when an aqueous solution of an enriched uranium compound was drained inadvertently into a waste drum having dimensions such that a chain reaction resulted.[16] Eight persons received general whole body doses from the radiations emanating from the critical system, five of these receiving total doses in excess of 200 rad. The technical aspects of this accident are covered in several reports. Brucer[17] and Andrews[18] have presented the clinical and laboratory findings in these cases.

Film badges were not worn by any of those exposed to the radiation field. Blood sodium activity was chosen as the most reliable measure of neutron and gamma doses in this accident. The neutron dose to a man at a given distance from the assembly was deduced from the Na^{24} concentration in his body by employing a phantom (in this case a burro). The phantom was exposed to the neutron field escaping from a "mock-up" reactor of dimensions and composition closely similar to those of the accident assembly. The blood serum Na^{24} level of the phantom resulting from irradiation by a measured first collision neutron dose was determined and was used to convert blood activity data to first collision neutron dose, assuming that the neutron spectrum did not vary with distance from the reactor. During another run of the same "mock-up" reactor, a measurement of the gamma-neutron dose ratio was made and was used to obtain the gamma doses. Table II shows the doses for the persons exposed. No deaths resulted from this exposure.

Yugoslavia Accident

In an accidental supercritical excursion of a zero-power reactor on Oct. 15, 1958, at the Boris Kidrich Institute of Nuclear Sciences at Vinca, near Belgrade, Yugoslavia, eight individuals were irradiated. Six of them received significant doses of neutrons and gamma rays.[19-21] One man died as a result of the irradiation. Clinical studies of the six acutely irradiated patients are reported by Jammet et al.[19] and hematological findings by Mathé et al.[22]

Although only incomplete information is available concerning the neutron and gamma leakage spectrum from the reactor and the disposition of people and apparatus at the time of the accident, it is possible to make estimates of the doses from Na^{24} activation data for the six patients treated at the Curie Foundation in Paris. These dose estimates, ranging from 640 to 350 rad, are presented in Table II.

Los Alamos Accident, LASL III

The most recent radiation accident occurred on Dec. 30, 1958, at the Los Alamos Scientific Laboratory.[23-25] In the course of a routine plutonium salvage operation, the material attained a critical state. A man (Case LA11) who was standing in close proximity to the critical system received a lethal dose.[23, 24]

The dose to the middle of his body is thought to be distinctly higher than that to other portions of his body. The Na^{24} activity found in his body may be used to obtain a whole-body average dose from previously described calculations. The fast neutron dose was estimated to be 2,200 rad and the gamma ray dose to be 6,600 rad.

Part II. Analysis of Past Accidents —Clinical Aspects

The Clinical Manifestations of the Radiation Syndrome

The clinical characteristics of the acute radiation syndrome in man have been learned from radiation accident cases, radiation therapy patients, and the casualties of atomic bombing. Although variations in types of radiation given, in the health of the recipients, and in the feasibility of valid, controlled clinical observations all serve to confuse the outlines of a clear-cut symptom complex, certain landmarks emerge. These have been compiled and reviewed by many authors, including a recent summary by Gerstner.[26]

The general concensus is that when man is exposed to a single whole-body dose of ionizing radiation, he exhibits certain clinical signs, symptoms, and laboratory findings which are collectively termed the radiation syndrome. The frequency and severity of occurrence of these manifestations are roughly related to the dose received and the sensitivity of the indi-

vidual patient. Exposures to less than 100 rad rarely result in clinical symptomatology; hence for our present purposes the radiation syndrome may be thought of as those clinical findings associated with total-body doses of radiation of over 100 rad.

The typical chronologic sequence of events following a large whole-body radiation exposure can be divided into four clinical stages: the initial or prodromal stage, the latent stage, the manifest illness stage, and the recovery stage. The prodromal clinical findings include anorexia, nausea, vomiting, extreme sweating, fatigue, and prostration. These changes remit in the latent period, which begins about two days later. After about two to three weeks of well-being a number of developments begin within a short time of one another. These may include fever, overt or occult infections, scalp hyperesthesia and epilation, purpura and hemorrhage, diarrhea, ileus, cardiovascular collapse, severe lethargy, and changes in sensorium. By about the end of the sixth week after exposure the situation has usually been resolved and clinical improvement of the surviving patients is rapid, although fatigue may continue for some time.

DOSE-RESPONSE RELATIONSHIPS—About 15% of patients exposed to a dose of 100 rad may be expected to show some of the signs and symptoms of the syndrome. The frequency increases sharply up to the level of approximately 200 rad, at which level most of those exposed would be expected to exhibit some clinical symptomatology.

The occurrence of fatalities has been considered generally to begin at about 200 rad, increasing to 50% at about 450 to 500 rad. The findings of this survey of radiation accidents do not substantiate these estimates, probably as a result of therapeutic intervention. Death did not occur in any of these treated patients with known exposure to less than 500 rad. The LD_{50} is impossible to estimate on the basis of the small amount of such data accumulated thus far. A fatal outcome is probably inevitable at about the 800 rad dose level.

RADIATION INJURY GROUPS—In spite of the implication in the foregoing paragraph, and in the radiobiological literature, that there is a useful relationship between magnitude of exposure dose and severity of clinical sequelae, it is considered essential to approach the problem of individual patient management from a somewhat different standpoint. This is necessitated in part by the difficulty in obtaining quick and accurate dose estimates in accident situations which are usually very complicated. In addition, even if complete dosimetric information were available, the biological response of one individual to a known exposure would still differ from that of his confrère exposed under identical physical circumstances. We have, therefore, deemed it useful in the management of radiation accidents arbitrarily to divide patients showing various symptoms and signs of the acute radiation syndrome into five different "radiation injury" groups.

The five radiation injury groups are defined in terms of our present recognition and understanding of certain definitive clinical occurrences which have appeared in normal persons accidentally exposed to external, penetrating, whole body radiation overdosage. Briefly the pertinent characteristics of each group may be summarized as follows:

Group I: Most of these patients are asymptomatic; a few may have minimal prodromal symptoms.

Group II: These patients develop this acute radiation syndrome in a mild form. After transient prodromal nausea and vomiting, laboratory and mild clinical evidence of hematopoietic derangement dominates the picture.

Group III: A serious course occurs in these patients. Complications of hematological malfunction are severe and, in the upper part of the group, some evidence of gastrointestinal damage may also be present.

Group IV: An accelerated version of the acute radiation syndrome occurs. Complications of gastrointestinal injury dominate the clinical picture. The severity of hematopoietic disturbances are related to the length of survival time following exposure.

Group V: A fulminating course with marked central nervous system impairment occurs in this group.

The radiation injury group classifications of the accident cases mentioned in the preceding section are indicated in Table III.

HYPOTHETICAL CLINICAL CASE ILLUSTRATIONS—In order to establish basic points of reference and to provide a better appreciation of the relevant clinical characteristics and laboratory findings, we shall present herein a hypothetical case report containing the expected findings of a patient in each injury group. For the purpose of illustrating all of the possible characteristic phenomena, each case will be portrayed as having experienced all or most of these findings. It must be borne in mind, however, that the radiation syndrome is similar to any other clinical entity in that it is unusual for any individual case to show all of the "textbook" findings.

Group I: Hypothetical Patient 1, a 27-year-old male technician, was exposed to a total body dose

TABLE III—PATIENTS CLASSIFIED BY CLINICAL RADIATION INJURY GROUPS

Group	No. of Patients	Patients by Code			
I	14	LA2	A1	OR6	
		LA6	A2	OR7	
		LA7	A3	OR8	
		LA8	A4		
		LA9			
		LA10			
		LA12*			
II	8	LA4	R2	OR1	Y6
				OR2	
				OR3	
				OR4	
				OR5	
III	6	LA1	R1*		Y2
					Y3
					Y4
					Y5
IV	2	LA3			Y1
V	1	LA11			
Total patients	31				

* Insufficient data for complete profiles; not included in averages.

of 14 rad of fast neutrons and 39 rad of prompt gamma radiation. This exposure was experienced as the result of not employing certain safety features while performing an experiment with a low-power reactor.

When first seen by the facility physician in the dispensary, 10 minutes after the accident, the patient exhibited no clinical symptoms other than a moderate tachycardia and moist palms. Blood was immediately drawn for base-line blood counts and for Na^{24} activation measurements. Bed rest in the dispensary was advised, pending the report of the first estimations of the magnitude of the exposure. The patient became increasingly restless and apprehensive over the next two hours; and, since no reasonably accurate dose estimates were at that time available, it was thought advisable to hospitalize the patient.

The initial blood data, which included hematocrit, total leukocyte, total lymphocyte, total neutrophile, and platelet counts, and differential formula, were normal. One hour later, blood specimens were obtained for repeat counts, as well as base-line blood chemistry determinations. The latter were all within the normal range, and there was essentially no change in the counts. The patient's apprehension continued until four hours after hospitalization, at which time it had been definitely determined that his exposure was to less than 100 rad. The patient was informed of this estimate and appraised of the favorable clinical prognosis. His restlessness, tachycardia, and vasomotor symptoms disappeared almost immediately, and he was discharged from the hospital the next day.

He was observed in the outpatient department for the next month, during which time he was completely asymptomatic and showed no alterations in his laboratory findings. He then returned to work in a nonexposure area. Thereafter, he was observed at increasing intervals. At no time were there any clinical or laboratory manifestations that could be attributed to his radiation exposure. No abnormalities were noted in the bone marrow studies.

Group II: Hypothetical Patient 2, a 46-year-old male laborer, was exposed to 90 rad of fast neutrons and 240 rad of gamma rays in a criticality type of accident at a production facility. He was hospitalized almost immediately but at the time of admission felt perfectly well. The admission physical examination and laboratory findings were all within normal limits. About two hours later, he began to experience rather persistent nausea and vomited five times within the next 24 hours.

During the next four and one-half days, he exhibited no abnormal symptoms other than weakness and fatigue. His appetite remained hearty, and there were no gastrointestinal symptoms. An uneventful clinical course, except for persistence of the weakness and fatigue, was observed until Day 16, when the patient stated that his scalp was tender to the touch, especially over the occipital and right parietal regions. These were the areas most frequently in contact with his pillow. Very little further attention was given to this symptom until Day 18 when it was noted that frank epilation was beginning over these areas. The epilation continued, involving not only patchy areas of the scalp, but the hair on the chest, thighs, and legs as well. His epilation stopped on Day 29.

On Day 18 the patient complained of a severe sore throat. He had a temperature of 100.2° F. accompanied by a proportionate tachycardia. Physical examination revealed an acute follicular tonsillitis with accompanying cervical adenopathy. It should be noted from Figure 1 that there was no leukocyte response to this infection. The erythrocyte sedimentation rate increased to 32 mm. This rise preceded the clinical infection by 24 hours. Throat cultures were made and the patient was immediately started on crystalline procaine penicillin in 600,000 unit doses, intramuscularly, every six hours. There was a temperature spike in the afternoon to 104.6° F. This was preceded by a rigorous chill lasting approximately 20 minutes. The patient's throat became so sore that he was unable to swallow even sips of water. His fever was reduced with sponge baths and large doses of acetylsalicylic acid (aspirin) per rectum. Two liters of 5% dextrose in saline were administered intravenously through the afternoon and evening. There were two more episodes of chills and hyperpyrexia during the next 12 hours. It then became evident that the patient had an early peritonsillar abcess.

The growth from the throat culture was identified as an alpha-hemolytic Streptococcus, and tube sensitivity studies revealed a high sensitivity of the organism to tetracycline and a relative resistance to penicillin. He was then started on a continuous slow intravenous infusion of 1 gm of tetracycline in saline, over a 24-hour period. The

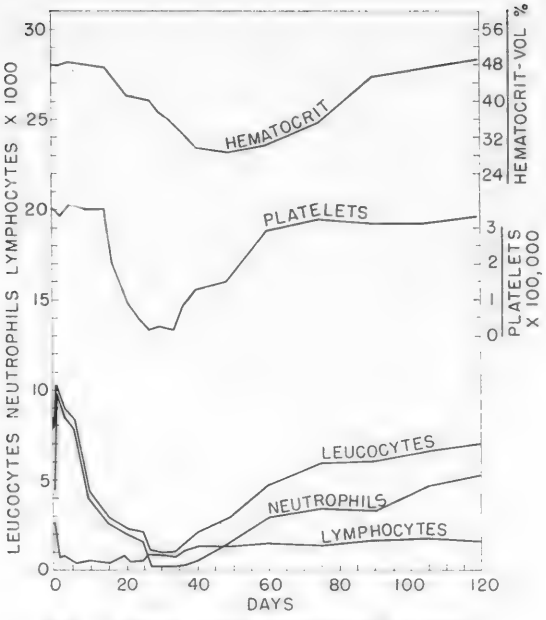

Fig. 1—Blood counts, hypothetical patient 2.

tetracycline was then continued by intramuscular injections of 100 mg every six hours. During the night of the 20th day, the abscess drained spontaneously and the patient was afebrile on the following morning. He tolerated a liquid diet in sufficient amounts to maintain a satisfactory intake without the use of parenteral fluids. By Day 23, there was complete clinical recovery and the antibiotic therapy was discontinued.

On Day 22, the platelet count began a progressive fall to a level of only 20,000 on Day 26. It remained at essentially that level until Day 30, on which a stepwise recovery began and was complete by Day 27. Paralleling the thrombocytopenia, but delayed by three days in its onset, there was a progressive fall in the leukocyte count, reaching a level of 850 on Day 32. The absolute lymphocyte count decreased from Day 27 to a level of 275 on Day 30. A slight reduction in the hematocrit also paralleled the other cytopenias. Purpura appeared first on the lower extremities on Day 25 and became generalized by Day 30. On Days 27 and 28, the patient noted that his gums bled when he brushed his teeth. Microscopic hematuria was also noted on Day 28. There was no other evidence of hemorrhage. During this period there was marked hypocellularity of the bone marrow. Hematological findings are presented graphically in Figure 1.

During the first 45 days, the patient lost 14 pounds. The clinical course from then on was uneventful. There was complete clearing of his purpura and a stepwise return to normal levels of all of the components of his hemogram by Day 60. It is interesting to note, however, that his sedimentation rate remained elevated for eight months. There was complete restoration of hair growth by the end of the third postexposure month. The patient's weakness and fatigue gradually diminished and he returned to light work in a nonradiation area five months after the accident. Periodic follow-up over the next three years failed to reveal any significant clinical or laboratory abnormalities, except for the persistent elevation of the sedimentation rate for eight months.

Group III: Hypothetical Patient 3, a 37-year-old male worker, received an estimated total body dose of 182 rad of fast neutrons and 536 rad of prompt gamma radiation in a criticality type of reactor accident.

He experienced no immediate reactions to this exposure; however, within a few minutes after his arrival at the hospital admitting room, approximately 45 minutes after the accident, he became nauseated and experienced violent retching and vomiting, perspired profusely, and felt extremely weak. Initial physical examination failed to reveal any significant abnormalities other than a moderate tachycardia, sweating, and a slightly increased respiratory rate. The rectal temperature was normal, as was the blood pressure. Blood and urine samples were obtained immediately for complete blood counts and base-line biochemical values, urinalysis, and Na^{24} measurement. The initial blood counts and urinalysis were within normal limits.

During the next 12 hours of his hospitalization, the patient continued to have nausea and vomiting. The sweating subsided, but the weakness persisted. A second blood count, made on the 12th hour, revealed a normal hematocrit and a normal platelet count. The total leukocyte count was elevated to approximately 13,000, almost all of which were neutrophils. The lymphocyte count had fallen to 800. A temperature elevation to 100° F. was noted.

A mild generalized erythema was noted toward the end of Day 1. The patient also complained of vague sensations of numbness of the upper extremities. The initial symptoms of anorexia, nausea, vomiting, weakness, erythema, and low-grade fever persisted.

There was a somewhat abrupt remission of these initial symptoms toward the end of Day 4. His appetite returned and he was essentially asymptomatic for the next nine days. The weakness, low-grade fever, and excessive sweating, however, persisted throughout this period. On Day 14, there was a sudden temperature elevation to 103° F. Physical examination revealed an acute pharyngitis accompanied by a diffuse hyperemia of the gums and buccal mucosa. Anorexia returned with the onset of this infection. A throat culture was made and antibiotic therapy was immediately initiated. He was given intramuscular doses of 600,000 units of penicillin, and 0.5 gm of steptomycin every six hours. There was a progressive temperature rise over the next 18 hours, reaching a level of 104.5° F. Early ulceration was noted in the pharynx. The hyperemia of the gums became marked. There was slight loosening of the teeth. Tube antibiotic sensitivity studies of the throat culture material revealed the pathogen to be most

sensitive to tetracycline, which was immediately administered by continuous intravenous drip. A total of 1 gm was given by this method over the next 24 hours. The penicillin and streptomycin were also continued. The temperature dropped precipitously to its previous level of approximately 100° F. on Day 17. The tetracycline was then administered orally in 250 mg doses every 6 hours. Elevation of the sedimentation rate, first noted on Day 12, decreased slightly at this time.

At the same time, Day 17, beginning epilation of the scalp was noted. The patient experienced pain and bleeding of the gums when brushing his teeth. From this time on, until death on Day 29, all stool examinations revealed occult blood. Purpura of the oral mucosa and skin of the trunk was first noted on Day 19. This became generalized, and during the terminal stages of the illness multiple large ecchymotic areas of the skin were present.

Bone marrow biopsy revealed almost complete acellularity, which was reflected in the peripheral counts by a profound pancytopenia. Figure 2 provides a graphic illustration of all blood counts. By Day 23, the patient's general condition had progressively deteriorated to the point that he was prostrate with profound weakness, lethargy, and intermittent disorientation. The total urinary output was reduced to less than 400 cc per 24 hours. This oliguria persisted until death. Fresh whole blood and platelet transfusions were administered over the next four days.

Diarrhea, accompanied by abdominal pain and cramps, began on Day 25 and increased in severity until Day 28, at which time massive hemorrhage from the lower gastrointestinal tract ensued. There were also continuous oozing of blood from the gums and one episode of hematemesis. Microscopic hematuria was also observed.

There was almost complete epilation of all of the hair of the body by this time. Early on Day 29, further severe bleeding from the lower gastrointestinal tract began. The patient went into profound shock, became comatose, and, in spite of vigorous transfusion therapy, died during the latter part of Day 29.

Group IV: Hypothetical Patient 4 was a 31-year-old male scientist who received a total body exposure to fast neutrons and gamma rays in a criticality reactor accident. It was estimated that his exposure resulted in a dose of 124 rad of fast neutrons and 830 rad of gamma rays. He immediately ran from the reactor building and was taken to the laboratory dispensary. He experienced nausea, vomiting, and retching 30 minutes after the exposure. He was hospitalized immediately. The nausea and vomiting increased in severity and frequency during the next four hours. During the third hour, he experienced severe intermittent abdominal cramps followed by two watery bowel movements within a period of 20 minutes. He was weak and prostrate, but there was progressive improvement, and by the 16th hour he had entered the latent phase of relative clinical well-being. He had a low-grade fever during the first 24 hours. On Day 1, there was an

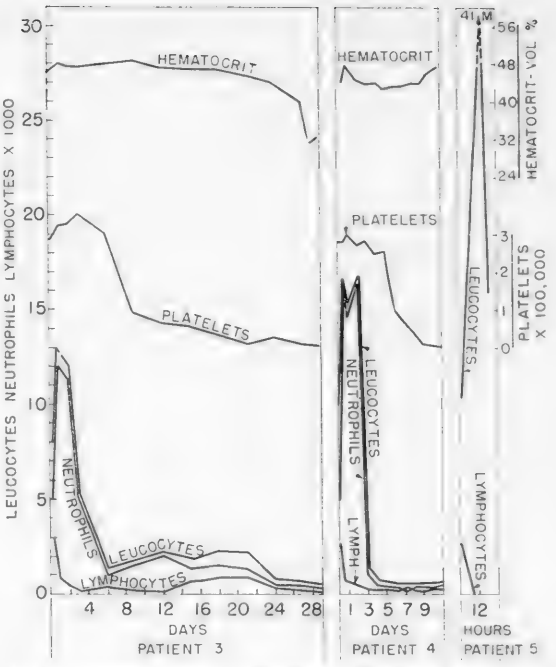

Fig. 2—Blood counts, hypothetical patients 3, 4, and 5.

initial leukocytosis, almost all of which was due to an increase in neutrophils as his absolute lymphocyte count fell to 600. His leukocytosis persisted. The lymphopenia was progressive, reaching a level of 250 on Day 3. Throughout the remainder of his illness, the absolute lymphocyte count never rose above this level.

Except for a continuation of his fatigue and a temperature elevation to 100.5° F. on Day 2, he was asymptomatic for the next five days. The low-grade fever persisted until Day 7.

About noon of Day 7, there was a recurrence of his nausea, vomiting, and watery diarrhea. This was accompanied by a rise in temperature to 103.2° F. and a corresponding elevation in the pulse rate. Almost simultaneous with the onset of these clinical symptoms, there was a precipitous fall in the cellular elements of his peripheral blood. The total leukocyte count decreased to 1,200, with a corresponding fall in the neutrophils. The platelet count decreased from its previous normal levels to 120,000. Hematologic results are shown in Figure 2.

The nausea and vomiting became increasingly severer, and early on Day 8 nasal gastric suction was established. There was also an increase in the severity of the diarrhea. Parenteral administration of fluids and electrolytes as well as whole blood was started, and he was placed on intramuscular penicillin and streptomycin. His temperature reached a high of 103.8°F. and the blood count showed 300 leukocytes and 80,000 platelets. There was hypocellularity of the bone marrow. On Day 9, his condition was essentially unchanged.

On the 10th day, the frequency of the diarrhea increased and the watery stools became bloody.

His temperature rose to 104° F. and his pulse was rapid and weak. Extreme prostration ensued; he was cyanotic, and his respirations were shallow and rapid. Tetracycline was given intravenously, and he was placed in an oxygen tent. In spite of whole blood transfusions, the shock became more profound. For a few hours, the circulatory collapse was successfully overcome with intervenous methoxamine HCl (Vasoxyl); however, early on Day 11, the temperature rose to 105.8° F., the shock again became profound, and he died.

Group V: Patient 5, a 37-year-old production specialist, received an estimated total body exposure to 2,000 rad of fast neutrons and 5,000 rad

TABLE IV—TIME OF ONSET AND DURATION OF

Group	I																
	LA2	LA6	LA7	LA8	LA9	LA10	LA12	A1	A2	A3	A4	OR6	OR7	OR8	LA4	R2	OR1
Anorexia	....	....	....	....	*6*a(<1)	....	....	*6(1)*	....	3(1)	....	....	....	....	*6(12)*	*1*(4)	*2*(5)
Nausea	....	....	....	....	*6*a(<1)	....	....	*6(1)*	....	3(1)	....	....	....	*2*(1i)	*6(12)*	*1*(4)	*2*(5)
Vomiting	....	....	....	....	....	....	....	*6(1)*	....	3(1)	....	....	....	....	*6(1)*	*1(4)*	*2*(2)
Diarrhea	....	....	....	....	....	....	....	....	....	3(1)	....	....	....	....	....	....	....
Abdominal pain	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Conjunctivitis	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Erythema	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Fever	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Sweating	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Oliguria	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Weakness*	....	....	....	....	....	....	....	....	....	....	....	....	....	*2*(1)	1(70)	*1*(4)	....
Prostration	....	....	....	....	....	....	....	....	....	....	....	....	....	....	1(10)	*1*(4)	....
Hyperesthesia	....	1(<1)	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Paresthesia	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Ataxia	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Disorientation	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Shock	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Coma	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Death	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....

Arabic number indicates postirradiation day of onset.

Arabic number *in italics* indicates postirradiation hour of onset.

Number in (parentheses) indicates duration.
* Includes fatigue.
† Limited to burned areas of upper extremities.
a Approximate time.
i Intermittent.

TABLE V—TIME OF ONSET AND DURATION OF CLINICAL

Group	I																
	LA2	LA6	LA7	LA8	A9	LA10	LA12	A1	A2	A3	A4	OR6	OR7	OR8	LA4	R2	OR1
Anorexia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	6(5)	24(20)	..
Nausea	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Vomiting	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Diarrhea	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Abdominal pain	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Adbominal distention	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Conjunctivitis	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Erythema	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Jaundice	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Fever	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5(6)	24(9)	31(3)
Infection	..	..	..	..	..	..	..	..	..	..	..	..	..	6(2a)	..	..	31(3)
Purpura	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	24(20a)	25(4)
Hemorrhage	..	..	..	..	..	..	..	..	..	..	15(<30)	..	..	..	..	24(20a)	25(2)
Scalp pain	..	..	..	..	..	..	..	..	..	..	..	..	..	..	17(>2)	13a(—)	16(4a)
Epilation	..	..	..	..	..	..	..	..	..	..	..	..	..	..	18(<30)	13(—)	17(27)
Sweating	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Oliguria															..	..	..
Weakness*	3(60)	..	..	..	..	..	..	..	..	17(16)	..	..	..	..	1(70)	24(20)	30a(56a)
Prostration															..	..	..
Weight loss	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1p(20)	NA	1p(6)
Hyperesthesia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Paresthesia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	15(10)	.	..
Ataxia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Disorientation	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Shock	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Coma	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Death	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Cataract left	..	..	..	..	..	..	..	..	..	..	..	..	..	..	32 mo.	..	..
right	..	..	..	..	..	..	..	..	..	..	..	..	..	..	58 mo.	..	..

Arabic number indicates post irradiation day of onset.
Arabic number *in italics* indicates post irradiation hour of onset.
Number in (parentheses) indicates duration.
* Includes fatigue.
† Patient had history of intermittent abdominal discomfort for several years.
‡ Epistaxis also occurred on day 14.
§ Epistaxis also occurred on day 12.
¶ Episode of supraventricular tachycardia. (History of previous episode.)
a Approximate time.
i Intermittent.
m Minutes.
p Presumed.

of gamma rays. By a complex series of technical errors, a large volume of enriched uranium in a liquid form was allowed to become supercritical.

The patient stated that he immediately felt a burning sensation over his entire body. He was able to stagger out of the building and attempted to reach a vehicle parked on the road. A maintenance man working across the road stated that he staggered aimlessly about like a drunken man for a minute or so and then collapsed on the ground. He began to retch violently within eight minutes after the exposure. He attempted to walk to the ambulance but was markedly ataxic and confused.

Clinical Signs and Symptoms—Initial Stage

II							III				IV		V
OR2	OR3	OR4	OR5	Y6	LA1	R1	Y2	Y3	Y4	Y5	LA3	Y1	LA11
2(1)	2(4)	4(3)	2(2)	1(1)	1(2)	1(3)	1(2a)	1(2a)	1(2a)	1(2a)	1(<1)	1(2a)	15m(35)
2(<1)	2(4)	4(3)	2(2)	1(1)	1(2)	1(3)	1(2a)	1(2a)	1(2a)	1(2a)	1(<1)	1(2a)	15m(35i)
....	2(4)	4(2)	2(6)	....	1(1)	1(3)	1(2a)	1(2a)	1(2a)	1(2a)	1(<1)	1(2a)	15m(35i)
....	....	....	....	....	....	....	....	....	....	....	4(1)	4(—)	45m(35i)
....	....	....	....	....	....	....	....	....	....	....	....	....	30m(1)
....	....	....	....	1(—)	....	....	1(—)	1(—)	1(—)	1(—)	—(—)	1(—)	30m(35)
....	....	....	....	....	....	....	1(14)	1(14)	1(14)	1(14)	1(9)	1(14)	30m(35)
....	....	....	....	....	1(24)	....	....	....	....	....	1(9)	....	30m(12)
....	....	....	....	1(>90)	....	....	1(>90)	1(>90)	1(>90)	1(>90)	....	1(31)	30(5)
....	....	....	....	....	....	....	....	....	....	....	1(2)	....	<1a(35)
....	....	....	....	1(>120)	1(24)	1(4)	1(>120)	1(>120)	1(>120)	1(>120)	1(1)	1(31)	5m(35)
....	....	....	....	....	1(1)	1(4)	....	....	....	....	1(1)	....	5m(35)
1(<1)	....	....	....	....	1(24†)	....	....	....	....	....	1(9†)	....	1m(35)
....	....	....	....	1(2a)	1(1†)	....	1(2a)	1(2a)	1(2a)	1(2a)	1(—†)	1(2a)	....
....	....	....	....	....	....	....	....	....	....	....	....	....	1m(35p)
....	....	....	....	....	....	....	....	....	....	....	....	....	1m(35p)
....	....	....	....	....	....	....	....	....	....	....	....	....	30ma(35p)
....	....	....	....	....	....	....	....	....	....	....	....	....	33(2)
....	....	....	....	....	....	....	....	....	....	....	....	....	35

m Minutes.
p Presumed.
t Includes terminal recurrence.
— Known to have occurred, but time unknown.
> More than, or later than.
< Less than, or earlier than.
NA Specific information about occurrence not available.
Leaders (....) indicate nonoccurrence.

Signs and Symptoms—Manifest Illness Stage

II					III						IV		V
OR2	OR3	OR4	OR5	Y6	LA1	R1	Y2	Y3	Y4	Y5	LA3	Y1	LA11
..	..	..	..	..	10(9t)	19(17)	30(6)	24(6)	30(6)	32(7)	6(4)	22(11)	15m(35)
..	..	..	..	..	10(9t)	..	30(6)	24(6)	30(6)	32(7)	6(4)	22(11)	15m(35)
..	..	..	..	..	17(1)	..	..	..	..	..	6(4i)	..	15m(35)
..	..	..	..	..	12(15)	..	..	..	..	..	7(3i)	..	45m(35)
..	24(1)†	..	..	21a(—)	10(4a)	..	31(6a)	29(6a)	29(6a)	29(6a)	6(4i)	22(9i)	..
..	..	..	.	..	10(4a)	..	..	..	..	29(6p)	6(4i)	22(9i)	..
..	..	..	..	..	14(4a)	..	..	..	..	..	..	..	<0.5(35)
..	..	..	..	..	3(23)	..	..	..	..	..	1(9)	..	<0.5(35)
..	..	..	..	..	25a(1p)	..	..	..	..	39(1a)	9(1t)	24(9a)	..
..	..	13(1)	..	..	1(25)	19(17)	21a(14ai)	21a(14ai)	21a(14ai)	21a(14ai)	1(9)	4(10it)	<0.5(35)
10(10)	..	10(34a)	3(10)	..	10a(13t)	19(17a)	31(—)	29(—)	29(—)	29(—)	..	NA	..
25(5)	..	..	..	..	..	19(22)	..	..	..	26(14)	..	..	..
..	..	..	26(2)	—(—)	..	19(22)	26(18)	26a(20a)	26a(20a)	26a(20a)	..	27(6‡)	..
..	16(4a)	..	16(4a)	..	..	..	..	..	..	..	..	..	..
17(14)	17(>27)	17(10)	17(14)	20(<90)	17(10)	NA	14(<90)	16(<90)	18(<90)	17(<90)	..	14(18)	..
..	..	..	..	1(>90)	..	19a(>22)	1(>90)	1(>90)	1(>90)	1(>90)	..	1(32)	30(5)
..	..	..	..	..	..	..	30(6a)	24(7a)	30(6a)	32(7a)	8(2)	24(9a)	<1a(35)
30a(56a)	44a(42a)	44a(42a)	44a(24a)	1(>120)	1(25)	19(22a)	1(>120)	1(>120)	1(>120)	1(>120)	1(9)	1(>120)	5m(35)
..	..	..	..	..	6(21)	19(22)	30(6)	24(7)	30(6)	32(7)	6(4)	24(9)	5m(35)
..	1p(4)	1p(5)	..	>10(>120)	1p(25)	NA	1(<120)	1(>118)	1(>118)	1(<106)	1(9)	1(32)	1p(35p)
..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	1m(35)
..	..	..	..	..	21a(4a)	..	..	..	..	..	7(3)	..	1m(35)
..	..	..	..	..	15(1)	..	..	..	..	..	8(2)	NA	<0.5(35)
..	..	..	..	..	25(1)	..	..	..	..	..	8(2a)	NA	33(2)
..	..	..	..	..	25	..	..	..	..	..	9	32	35
..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..

t Includes terminal recurrence.
— Known to have occurred but time unknown.
> More than, or later than.
< Less than, or earlier than.
NA Specific information about occurrence not available.
Leader (..) indicates nonoccurrence.

On admission to the hospital, 20 minutes after exposure, the patient was vomiting and had an explosive involuntary watery bowel movement. He was cyanotic and in acute respiratory distress. A generalized erythema was noted, and he was in clinical shock as evidenced by a blood pressure of 70/50. Vigorous therapy with whole blood transfusions was employed but failed to combat the clinical shock. Intravenous methoxamine HCl (Vasoxyl) was begun during the fourth hour. The response to this therapy was insufficient to raise the patient's blood pressure out of the range of clinical shock. The vomiting and confusion persisted. The sensorium remained clouded. On the 10th hour, 90 cc. of urine was obtained by catheterization, indicating that there was an almost complete anuria from the onset. By the 16th hour, prostration was marked. The patient became progressively more disoriented, and twitching of various muscles was noted. He became comatose in the 21st hour, convulsed, and died a few minutes later.

The blood counts made during the first hour were normal in every respect. Blood taken hourly for counts revealed a progressive increase in the leukocyte count to a level of 41,000 in the 16th hour followed by a steady decrease to the level of 16,000 just prior to death. By the third hour, the lymphocyte count had decreased to 950, and by the seventh hour there was a complete disappearance of lymphocytes from the peripheral blood. The findings of the bone marrow biopsy made during the early hours were not remarkable. Hematological data are presented graphically in Figure 2.

Only 180 cc. of urine was obtained from the time of the initial catheterization until death. Consistent with this oliguria, there was a steady rise in the NPN and BUN levels reaching 82 and 19 mg % respectively.

Analysis of Accident Cases

The hypothetical cases just presented were developed from the data contained in reports of the accident cases reviewed in this section. In Table III the actual cases are classified by radiation injury groups. We shall now consider the clinical data in these cases.

CLINICAL SIGNS AND SYMPTOMS — The time of onset and of duration of clinical signs and symptoms in the early postirradiation period are given in Table IV. A similar compilation in Table V presents the clinical phenomena of the stage of manifest radiation illness. Where an early finding disappeared and then recurred after the latent period, it has been handled as a newly occurring finding. If, on the other hand, it persisted from the start, it has been recorded identically on both tables. Great variations in the observations made, the clarity with which they were reported, the many forms of therapy employed, and the small number of cases involved make these data a somewhat imprecise basis from which to reach firm diagnostic and prognostic conclusions. Nevertheless, certain generalizations appear warranted.

Initial Stage—The classic prodromal gastrointestinal symptoms of the acute radiation syndrome, i.e., anorexia, nausea, and vomiting, were present in all patients in Group III and above, within an hour after exposure. They generally continued for about two days. In Group III, the triad was somewhat slower in appearing, beginning within six hours, but continuing intermittently for about the same duration. Two of the eight patients did not vomit at all. Only 4 of the 14 Group I patients had anorexia or nausea, and only 2 of them vomited. In one of these, the symptoms occurred on the third day and were considered by the physician in charge as "a manifestation of anxiety and tension rather than radiation sickness."

The occurrence of diarrhea in this stage seemed to be of serious prognostic importance. Other than in the previously mentioned patient in Group I who had the anxiety reaction, this symptom occurred only in the Group IV and V cases, all three of which were fatal. It appeared on Day 4 in both Group IV patients. In the Group V patient it started in 45 minutes, shortly after the onset of abdominal pain.

Weakness and fatigue were found in occasional Group I and II cases but were present and prolonged in *all* cases above that level of injury. Early prostration was also sometimes noted for a short time in Group II and above.

Other symptoms which were frequent almost exclusively in Group III and above included conjunctivitis, erythema, sweating, and paresthesias. Oliguria was seen in only one Group IV case and the Group V case.

Immediate central nervous system symptomatology, including ataxia, disorientation, and cardiovascular collapse, were seen only in the latter patient. He later became comatose and died about 36 hours after radiation exposure with no evident latent period after the start of his illness. All other patients did have a variably long period of remission of early symptoms before the manifest illness stage began.

Manifest Illness Stage—Patients in Group I showed no clinical evidence of illness of any kind after the initial stage subsided, except for one upper respiratory infection, one small retinal hemorrhage, and two complaints of weakness.

The most frequent finding above Group I was weakness and fatigue. This occurred in all cases. Onset in Group II was most often in the fifth or sixth week. In Group III and above it appeared almost immediately. Duration was variable, but generally the symptom lasted for several months.

TABLE VI—PROFILE VALUES ASSIGNED FOR VARIOUS RANGES OF ABNORMALITY
HEMATOLOGY—PERIPHERAL COUNTS

Test	Units	Normal*	Profile Value (For increase above:) 1	2	3	4	Profile Value (For decrease below:) 1	2	3	4
Hemoglobin	Gm.%	M-15.8	18	19	20	21	14	12	10	8
		F-13.9	16	17	18	19	11.5	10	8.5	7
Erythrocytes	Mill/mm³	M-5.4	6.0	7.0	8.0	9.0	4.5	3.5	2.5	1.5
		F-4.8	5.5	6.5	7.5	8.5	4.0	3.0	2.0	1.0
Hematocrit	Vol.%	M-47	54	56	58	60	40	35	30	25
		F-42	47	49	51	53	37	32	27	22
Leucocytes	1000/mm³	7.4	12	18	24	30	4.0	3.0	2.0	1.0
Neutrophils	1000/mm³	4.4	7.7	14	21	28.0	1.8	1.3	0.9	0.5
Lymphocytes	1000/mm³	2.5	4.8	7.0	10	12.0	1.0	0.75	0.5	0.3
Platelets	1000/mm³									
Rees-Ecker		405	545	700	850	1000	273	200	100	30
Brecher-Cronkite		257	440	600	750	900	140	100	50	30
Fonio		234	350	500	650	800	130	100	50	30
Dameshek		716	900	1000	1500	2000	500	350	100	30
Reticulocytes	% RBC	1.5	4	8	15	25	.5	0		
Erythrocyte Sedimentation Rate	mm/hr.	M-5	10	20	30	40				
		F-10	20	30	40	50				

* Expressed as "universal mean" value—taken from Albritton.[25]

Another common finding in all groups above the first one was epilation. Time of onset ranged from 13 to 20 days, with 10 of 14 patients beginning to lose hair between the 16th and 18th days. Two other patients, dying in one and one-half and in nine days, did not epilate. No data are given in the remaining case. No clear relationship of time of onset or of duration to injury group is evident.

Scalp hyperesthesia or pain occurred in most Group II patients one or two days before epilation. No similar finding was noted in the higher groups.

Sporadic episodes of fever were observed in half of the patients in Group II and in all of those above that group. These were of short duration in Group II, but lasted one or more weeks in most of the more injured patients.

Clinical evidence of infection was seen between the second and fourth weeks in half of Group II, including two of the four febrile patients. In Group III all cases showed such indications. Definite clinical infection was not noted in Groups IV and V.

Hemorrhagic phenomena, such as gingival bleeding, epistaxis, petechiae, and purpura, were observed in most cases of Group II and above who survived beyond the third week. Serious hemorrhage was limited to two patients in the fourth postexposure week. One, in Group III, had menorrhagia and another in Group IV died with uncontrollable hematemeses and, finally, hemoptyses.

In Group III and above a number of symptoms including recurrent anorexia and nausea, abdominal discomfort, prostration, and oliguria appeared at the peak of manifest illness. These findings occurred earlier in the more acutely ill patients, who also had the additional symptoms of vomiting, diarrhea, and abdominal distention. Disorientation, shock, coma, and death followed in several instances.

Jaundice was noted in mild transient form at the end of this period in two individuals in Group III and in more marked form terminally in the two Group IV patients.

Weight loss was mild and not of long duration in Group II. In higher groups it appears to have been severer but details are somewhat scant.

Subsequent cataracts have been observed in one member of Group II. No other long-term effects have been reported.

LABORATORY FINDINGS — A large number of laboratory examinations of many varieties were performed in the radiation accident patients discussed in this report. In order to consider and compare the laboratory observations, it was clearly necessary to develop a procedure for their analysis which would allow broad conclusions to be drawn despite differences in details of methodology employed in the diverse study centers.

The accepted normal range of results of each test procedure which was widely used among the cases under study, or which is recommended for such future use, was determined. A scoring system was then devised which assigned values from 1 to 4 to ranges of increasing deviation from the normal range. Using the resultant values, "profiles of injury" could be scored for the individual patients whose laboratory findings were so analyzed. These have been called "profile scores." The values assigned to

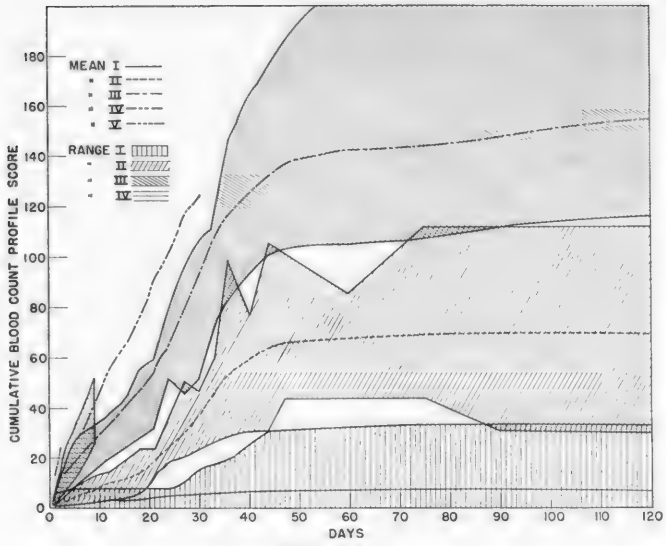

Figure 3

the various deviations of laboratory tests from the normal range have therefore been designated "profile values." The profile values for hematological tests are given in Table VI. Profile values for coagulation tests and for biochemical tests of urine and blood are published elsewhere.[29] Profile values were not assigned to tests which are not suited to this type of analysis.

Profile scores were determined for all possible tests in each individual case. These were analyzed individually and also cumulatively over the postexposure time period. Then, to facilitate intragroup comparisons, an attempt was made to determine the mean profile score for each radiation injury group on each type of test procedure at various convenient postexposure time intervals.

Unfortunately, it was found that only in the category of hematological tests were there a sufficient number of observations performed in uniform enough time periods in a large enough number of the accident patients to permit determination of mean profile scores for each clinical radiation injury group. It is possible, however, that profile scores for other tests might also be useful in the future, provided that they are performed at relatively frequent and consistent intervals. For this reason, suggested profile values for ranges of abnormalities of standard blood clotting, blood chemistry, and urine chemistry tests are given in another report.[29]

Peripheral Blood Counts—Previous reports have indicated the utility of one or another of the components of the peripheral blood count as an indicator of radiation injury.[11, 18, 30] Granulocytes, lymphocytes, monocytes, platelets, and reticulocytes have all been shown to contribute helpful information. We have reviewed the hematological data with two main questions in mind. One is how much they aid in the assignment of an unknown case to a specific injury group, with all the therapeutic and prognostic implications appertaining thereto. The other is how well they help to detect complications or therapeutic responses to the subsequent course.

Total blood count profile score is made up of scores for counts of erythrocytes or hematocrit, leucocytes, granulocytes, lymphocytes, and platelets. Other elements were omitted on the previously discussed grounds of infrequency and irregularity of tests.

When the means of such integral scores were cumulated by groups and graphed (Fig. 3) variations in the rate of accumulation of injury over time, and its maximum magnitude, were evidently closely related to the signs of clinical injury upon which injury group selection was based. It was possible to separate the mean score of cases falling into Group I and II from those of the sicker ones after 48 hours or less. Group V was also quite distinguishable from the outset. By the sixth day, Group I was distinct from II, and III from IV.

Examination of the ranges of the cumulative group mean scores portrayed in Figure 3 shows the value of the blood count in indicating radiation injury. It also makes clear the difficulty of relying solely on this measure in the initial stage of radiation illness when there is considerable overlapping of group mean profile score ranges.

If one wishes to refine the estimation of injury group assignment further, certain individual tests which go into the previous total scores may be considered individually. It must be realized, however, that the more data that can be compared with the mean scores herein, the greater the confidence that can be placed in the resultant prognostic conclusions.

The lymphocyte scores appeared to be the best prompt laboratory indicators of radiation injury. In 48 hours Groups II, III, IV, and V were well separated in mean score. However, a few of the Group II cases showed little early lymphocyte fall and the opposite occurred in Group I, so that there remained some overlapping of the two lower groups. If one considered the presence or absence of prodromal (nausea and/or vomiting) symptoms in addition to the

lymphocyte score in assigning patients to these two groups, the likelihood of correct decision was further enhanced.

The neutrophil score did not facilitate differentiation of Groups I and II. Nevertheless, it was useful supportive evidence in separating the two lower groups from the three higher ones by Day 3. Also Groups III and IV were becoming distinct on Day 3 by this means. However, Groups I and II were not separable for the first month.

The leukocyte score gave rather similar information but not as distinctly as did the neutrophil score. This was, of course, a reflection of the fact that neutrophil variations account for most of the white count changes, but lymphocyte shifts are also involved. Thus the distinction between Groups I and II was present earlier here than in the neutrophil score.

The platelet score was not very useful in the early days after exposure. However, the differentiation of Group IV from Group III was apparent by this test as early as Day 6. After the third week, sharp changes separated Groups II and III from the unaltered Group I.

Erythrocyte scoring was least helpful early. There was a reversal of Groups III and IV. However, a difference between Groups II and III was discernable after the first month. Therapeutic efforts, such as transfusion, and some preexposure abnormalities confused the data from this test.

Regarding the value of hematological profile scores as an indicator of complications no clear findings emerge. Neither infections nor bleeding began *only* when neutrophil or platelet levels were lowest, although this was generally so. Distinct deviations of an individual case from the group pattern during the course might indicate complications. However, more data are needed to define the ranges of the group patterns before this procedure can be evaluated adequately.

Reflections of therapy, other than that of transfusions already mentioned in the previous discussion of erythrocytes, may have occurred in the Yugoslavian cases. The Group IV data are based on Y6 alone after the death of LA3 on Day 9. The near normal neutrophil integral scores on Days 15 and 18 follow embryonal myeloid tissue transfusion, and the one on Day 30 follows adult marrow transfusion. The integral platelet score on Day 30 also is normal. Similar effects of marrow transplantation in cases Y2, Y3, Y4, and Y5, all in Group III, may be responsible for the improvement of that group's neutrophil and platelet scores somewhat earlier than those of Group II.

Other Hematological Tests—Bone Marrow: Examinations were made at various times in many of the cases. However, quantitation or codification of results is not possible; so no profile could be devised. Detailed discussions of bone marrow findings are given in several reports.[11, 15, 17, 18]

In general, relation of appearance of an aspirated sample of marrow to amount of injury or prognosis is not sufficiently obvious to use in making injury group assignments. There is a hypocellularity from the early period after exposure, with depression of the granulocytic series in particular. Mononuclear cells of the reticulum and plasma cell varieties remain, with variable concentrations of erythroid precursors. Megakaryocytic diminution and deterioration is present later. Regeneration of erythroid and myeloid precursors may develop in the face of falling peripheral counts and a subsequent fatal outcome.

Reticulocytes: Data were insufficient for profiling. Depression of levels was generally prompt, but depth was not clearly related to injury level. Recovery was indicated by reticulocytosis, with possible direct relationship of its height to the level of previous injury.[18]

Erythrocyte Sedimentation Rate: The results of this test were available serially only in the Oak Ridge cases. Here a close relationship of elevation to the early stages of infection seems to have been present. However, the abnormality persists far beyond the infection which it heralded. Further data would be useful in evaluating the apparent usefulness of this test as a warning of infection at a time when the usual signs, such as fever or leucocytosis, may not be of service.

Blood Coagulation Tests: The coagulation time was the test most consistently performed. Patients LA3, LA4, and LA6 showed significant prolongations. The maximum deviation of the latter two occurred on Day 6. In the case of LA3, a Group IV patient, there was a progressive prolongation of the clotting time. Just prior to death on Day 9, the blood was uncoagulable. An increase in clotting time was noted on many occasions in various patients from the Yugoslavian accident.

A variety of tests to measure components of the prothrombin complex were carried out in some of the cases. In general, there was no evidence of derangement, except in a few of the patients severely injured. The plasma prothrombin time was moderately increased in LA3. A decrease in Ac globulin and proconvertin was noted in Y2. The tourniquet test was positive on many determinations made on the Yugoslavian patients, especially patients

Y4, Y5, and Y6. Of the five Oak Ridge patients in Injury Group II, four had elevated levels of Ac globulin; all had distinctly elevated levels of antihemophilic globulin at the peak of their thrombocytopenia. These abnormalities of the plasma clotting factors are believed to be related, at least in part, to the thrombocytopenia.

Blood Chemistry—The blood electrolytes were measured in practically all of the patients, and failed to reveal any significant abnormalities, other than those associated with prolonged vomiting or diarrhea. Nitrogen retention was noted in all patients exhibiting oliguria. Calcium and phosphorus metabolism appeared to be unaltered, except in the case of LA3, in which there was a decrease in blood calcium, which would have been expected in a patient with severe nitrogen retention.

Total protein measurements and electrophoretic fractionation were carried out on practically all Group II, III, and IV patients. The results of these determinations were extremely variable and completely inconsistent. There was evidence of hyperbilirubinemia in patients LA3, LA1, and Y1, either terminally or at postmortem examination. A number of other biochemical procedures were carried out, none of which revealed any significant abnormalities.

Urine Chemistry — Urinary output was recorded for all patients except R1 and R2. In all Group III cases and above, except LA1, a decrease to oliguric levels was noted during the critical period of the manifest illness stage.

There were no significant effects in either total nitrogen, amino nitrogen, or uric acid excretion in the Group II Oak Ridge patients.

Quantitative determinations of urinary amino acids were made in most of the cases in all groups. Increased excretion of a variety of these was noted as early as 12 hours after irradiation, but there was no quantitative dose correlation. A newly discovered urinary amino acid, beta-aminoisobutyric acid (BAIBA), was excreted in increased amounts by the Oak Ridge patients in Group II.[17] Excretion was maximum during the first few days after exposure and returned to normal by Day 10. The magnitude of the increase in excretion of BAIBA in these cases appears to be related to dose.

Significant increases in bile pigment excretion was noted in LA3, LA4, and occasionally in some of the Yugoslavians. There was presumptive evidence of an increase in LA1. The increase in coproporphyrin excretion in LA4, a Group II patient, first occurred and was at the highest level on Day 2. It recurred intermittently through Day 13. An increase in urobilinogen was noted on Day 6 only.

Miscellaneous Observations — Bacteriology procedures carried out on a number of patients in all groups were not particularly helpful. Occult blood was found in the stools of several patients in Groups II and above at the time of other hemorrhagic manifestations.

Seminal fluid examinations made on the male Argonne patients showed an aspermia by the 10th month in A1, the patient who received the highest dose. In all of the surviving male Yugoslavian patients there were marked quantitative and morphologic changes in the sperm. At autopsy of Y1, a total depopulation of the seminiferous tubules was found. Similar findings were noted in LA1, and LA3 at autopsy. LA4 had aspermia at the seventh month which persisted for 17 months. Testicular biopsy in this patient revealed marked atrophy at the 10th month. Biopsy at 50 months after irradiation again revealed atrophy but there was evidence of partial regeneration.

Slit lamp examinations of the lens were made in most of the nonfatal cases. Only one, LA4, developed lens opacities. The first was noted in the left eye at 32 months after exposure, and by 58 months an incipient cataract in the lens of his right eye had developed.

Part III. Recommended Medical Procedures

The selection and time of performance of appropriate diagnostic and clinical procedures will be strongly influenced by three kinds of knowledge. The first is the clinical acumen and judgment which would be brought to bear on the medical management of any patient. The second is an awareness of the underlying pathophysiology of the acute radiation syndrome in man. The third is a general idea of the magnitude and type of radiation to which the patient has been exposed. Discussion of the first of these is beyond the scope of this paper. The next two have already been mentioned, but their application in the individual accidental exposure case warrants some further consideration.

In a given accident, the exposure dose would seem to be the logical piece of information which upon clinical management can be planned. As has already been indicated, however, it is not necessarily helpful in the individual case for two reasons: First, the dose, if it can be determined, is not usually available as soon as needed. Second, no given individual will necessarily respond exactly as his confreres in a given dose category. Therefore, the highest priority diagnostic recommendations in the early postexposure period are planned for the

accumulation of sufficient information to establish the response "profile" of the individual under study in comparison with those of others who were studied in a similar manner after whatever dose of radiation. When this information is available, a reasonably accurate prognosis can be made and planning of clinical management can proceed even in the absence of dosimetry information. It is highly desirable, of course, to obtain physical dosimetry data as soon as possible to supplement the clinical estimate of injury.

Subsequent tests will be recommended to serve four purposes: to validate the original diagnostic and prognostic conclusions in the patient; to detect promptly the development of clinical complications in the patient's course; to provide more data for improved profile scoring of future cases; and to supply more information about radiation pathophysiology.

Diagnostic Procedures

Given one or more individuals who have accidentally received, in all probability, a significant acute injurious radiation overexposure of neutron and/or gamma ray type, how should the attending physician proceed? It is rather obvious that in our present state of knowledge of human radiation injury there really is no procedure which might not be productive of some new information of immediate or eventual applicability. However, it is also obvious that diagnostic tests must include those that are most essential and none that are detrimental to the individuals involved. The resultant limitation in number and frequency makes a well-informed selection all the more important.

In the course of this analysis of all available criticality accidents, certain diagnostic hints have emerged which may aid in dealing with similar situations in the future. Further experience may alter these recommendations completely, but at this time the procedures listed in Table XII seem to be the most likely to facilitate preliminary clinical evaluation and subsequent management.

The diagnostic tests have been outlined in tabular form for convenience of the reader. Frequency and duration of test performances are given. Suggestions based on the analysis of previous studies are made for each of the five clinical injury groups. In line with the objectives of these diagnostic recommendations, test procedures have been categorized as Type A, B, or C. Type A procedures are of particular applicability in the early diagnostic and prognostic appraisal of clinical radiation injury. Type B procedures are of more help in confirming the earlier estimations of injury

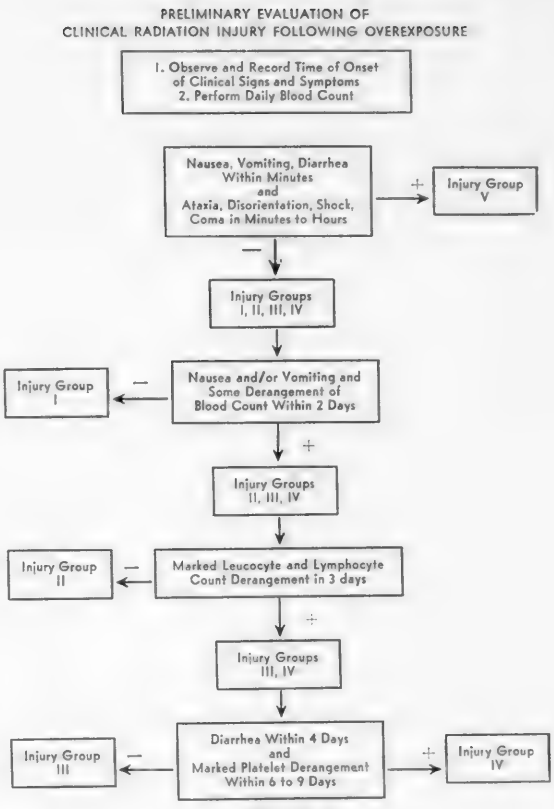
PRELIMINARY EVALUATION OF
CLINICAL RADIATION INJURY FOLLOWING OVEREXPOSURE
1. Observe and Record Time of Onset of Clinical Signs and Symptoms
2. Perform Daily Blood Count
Nausea, Vomiting, Diarrhea Within Minutes and Ataxia, Disorientation, Shock, Coma in Minutes to Hours
+
Injury Group V
—
Injury Groups I, II, III, IV
Injury Group I
—
Nausea and/or Vomiting and Some Derangement of Blood Count Within 2 Days
+
Injury Groups II, III, IV
Injury Group II
—
Marked Leucocyte and Lymphocyte Count Derangement in 3 days
+
Injury Groups III, IV
Injury Group III
—
Diarrhea Within 4 Days and Marked Platelet Derangement Within 6 to 9 Days
+
Injury Group IV

Figure 4

and in recognizing and managing the development of complications. Type C procedures are of possible but not yet verified value for future use in either of the two previous categories. In order to determine their suitability, they should be utilized when feasible.

While this procedural outline is thus segmented, somewhat arbitrarily, for the sake of clarity of presentation, it should be clearly understood that each individual case must be viewed and studied in its own right as the particular symptomatology and course require. It should also be recognized that it is beyond the purpose of this listing to include specific recommendations for future scientific lines of investigation of the acute radiation syndrome. Such radiobiological studies, while assuredly desirable, must emanate from the interest and availability of appropriate research personnel in each particular instance. For the purposes which have stimulated the preparation of this report it should suffice to point out that the accumulation of good basic clinical and laboratory data in a consistent and logical form from these unfortunate episodes will itself be a distinct contribution to radiobiological knowledge as well as a means of facilitating clinical patient management.

TABLE VII—BLOOD COUNTS AND PROFILE SCORING—HYPOTHETICAL CASE 3

Day	Hematocrit			Leucocytes			Neutrophils			Lymphocytes			Platelets			Total Score	
		Score			Score			Score			Score			Score			
	Vol %	D	C	Count	D	C	Count	D	C	Count	D	C	Count X 1000	D	C	D	C
1	48	0	0	13,000	1	1	12,100	1	1	800	1	1	320	0	0	3	3
2	47	0	0	12,100	1	2	11,200	1	2	290	4	5	330	0	0	6	9
3	47	0	0	5,300	0	2	5,000	0	2	100	4	9	350	0	0	4	13
4	47			3,900			3,700			150							
5				2,900			2,550			280							
6	48	0	0	1,400	3	5	1,060	2	4	260	4	13	300	0	0	9	22
7				1,550			1,300			200							
8				1,600			1,350			180							
9	48	0	0	1,700	3	8	1,500	1	5	150	4	17	90	2	2	10	32
10				2,000			1,800			100							
11				2,050			1,950			90							
12	47	0	0	2,100	2	10	2,000	0	5	90	4	21	60	2	4	8	40
13				2,050			1,700			300							
14				1,950			1,500			400							
15	47	0	0	1,950	3	13	1,250	2	7	650	3	24	50	2	6	10	50
16				2,050			1,280			760							
17				2,150			1,300			820							
18	47	0	0	2,250	2	15	1,350	2	9	880	1	25	40	3	9	8	58
19				2,250			1,300			900			30				
20				2,150			1,200			920			20				
21	45	0	0	2,100	2	17	1,150	2	11	950	1	26	10	4	13	9	67
22				1,750			1,000			750			20				
23				1,300			700			600			30				
24	44	0	0	900	4	21	550	3	14	300	3	29	50	4	17	14	81
25				850			500			250			30				
26				800			550			200			20				
27	39	1	1	750	4	25	600	3	17	100	4	33	10	4	21	16	97
28	31			600			500			84			10				
29	32	2	3	500	4	29	400	4	21	75	4	37	10	4	25	18	115

D Daily
C Cumulative

TABLE VIII—INTEGRAL AND CUMULATIVE RANGE

Day	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0	0	0	0	0–2	0.54	0–2	0.54	0–2	0.69	0–2	0.69
2	0	0	0	0	0–1	0.23	0–3	0.77	0–1	0.23	0–3	0.92
3	0	0	0	0	0–1	0.23	0–3	1.00	0–1	0.23	0–3	1.15
6	0	0	0	0	0–2	0.15	0–3	1.15	0–2	0.15	0–3	1.30
9	0	0	0	0	0	0	0–3	1.15	0	0	0–3	1.30
12	0	0	0	0	0–1	0.08	0–3	1.23	0–1	0.08	0–3	1.38
15	0	0	0	0	0	0	0–3	1.23	0	0	0–3	1.38
18	0–1	0.08	0–1	0.08	0	0	0–3	1.23	0	0	0–3	1.38
21	0–1	0.08	0–2	0.16	0	0	0–3	1.23	0	0	0–3	1.38
24	0–1	0.08	0–3	0.24	0–1	0.08	0–4	1.31	0–1	0.08	0–4	1.46
27	0–1	0.23	0–4	0.47	0–1	0.08	0–5	1.39	0–1	0.08	0–5	1.54
30	0–1	0.23	0–5	0.70	0–1	0.08	0–5	1.47	0	0	0–5	1.54
33	0–1	0.08	0–5	0.78	0–1	0.08	0–5	1.55	0	0	0–5	1.54
36	0–1	0.08	0–5	0.86	0–1	0.08	0–5	1.63	0	0	0–5	1.54
40	0–1	0.08	0–5	0.94	0–2	0.15	0–5	1.78	0–2	0.15	0–5	1.69
44	0–1	0.08	0–6	1.02	0–2	0.15	0–7	1.93	0–1	0.08	0–5	1.77
48	0–1	0.08	0–7	1.10	0	0	0–7	1.93	0	0	0–5	1.77
60	0–1	0.08	0–8	1.18	0	0	0–7	1.93	0	0	0–5	1.77
75	0–1	0.08	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77
90	0	0	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77
105	0	0	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77
120	0	0	0–9	1.26	0	0	0–7	1.93	0	0	0–5	1.77

PRELIMINARY EVALUATION OF RADIATION INJURY—An attempt has been made, utilizing the early clinical data recorded in the past accident cases, to identify those findings which have the greatest early prognostic value by indicating the correct injury group assignment and thus subsequent clinical course. On this basis a plan has been drawn up which should aid in planning for subsequent patient care. It is briefly summarized in Figure 4. This evaluation plan rests on the early and accurate performance of two familiar diagnostic procedures called for in Table XII — continuous detailed clinical observations and blood counts. The necessary clinical observations include a complete history of the immediate episode as well as of previous and preexisting abnormalities in health. A complete physical examination is indicated both to find any abnormalities present and to serve as a base-line observation for subsequent changes. Items of particular interest are the exact time of onset and duration of symptoms and signs listed in Table IV. Central nervous system and gastrointestinal findings are of greatest importance in the preliminary evaluation process.

The blood counts should include erythrocyte count and/or hematocrit, leukocyte count, differential count, calculated total lymphocytes and neutrophils, and platelet count. They should be performed at least once daily for the first three days. To evaluate the results, the blood count profile scoring method is recommended.

DIAGNOSTIC USE OF PROFILE SCORING METHOD —To demonstrate the use of the scoring method, the hematological findings of Hypothetical Case 3 are presented in Table VII. The leukocyte count on Day 1 is 13,000. On Day 2, a count of 12,100 scores 1 again. Thus the integral score again is 1, but the cumulative leukocyte score is now 2. These steps are carried out for all components of the blood count.

The integral and cumulative scores of individual counts and total counts are then compared with those presented as group mean scores and their ranges on Tables VIII, IX, X, and XI. The total cumulative scores of Hypothetical Case 3 for Days 1, 2, and 3 are 3, 9, and 13. Since the mean scores of Group III are 1.6, 7.6, and 14.0 while those of Group II are 1.4, 2.4, and 3.3, it appears that Hypothetical Case 3 is most likely to present a rather severe version of the clinical course of Group III. Referring to Figure 4, one also can narrow down this patient's injury pattern to that of Group III or IV. Further clinical and blood count data are needed to make a more definite distinction between Group III and IV. The amount of platelet derangement mentioned in Figure 4 can be determined by looking at the appropriate space in Table X.

It should be pointed out that when more frequent counts are performed than the recom-

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP I

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–1	0.23	0–1	0.23	0	0	0	0	0–4	1.46	0–6	1.46
0–1	0.15	0–2	0.38	0	0	0	0	0–2	0.61	0–6	2.07
0–1	0.08	0–2	0.46	0	0	0	0	0–3	0.54	0–7	2.61
0–1	0.23	0–2	0.69	0	0	0	0	0–4	0.53	0–8	3.14
0–1	0.15	0–3	0.84	0	0	0	0	0–1	0.15	0–8	3.29
0–1	0.08	0–3	0.92	0	0	0	0	0–2	0.24	0–8	3.53
0–1	0.15	0–4	1.07	0	0	0	0	0–1	0.15	0–8	3.68
0–1	0.15	0–5	1.22	0	0	0	0	0–1	0.23	0–8	3.91
0–1	0.15	0–6	1.37	0	0	0	0	0–1	0.23	0–8	4.14
0–1	0.15	0–7	1.52	0	0	0	0	0–2	0.39	0–8	4.53
0–1	0.08	0–8	1.60	0–2	0.23	0–2	0.23	0–4	0.70	0–11	5.23
0	0	0–8	1.60	0–3	0.23	0–5	0.46	0–5	0.54	0–16	5.77
0	0	0–8	1.60	0	0	0–5	0.46	0–2	0.16	0–18	5.93
0	0	0–8	1.60	0	0	0–5	0.46	0–2	0.16	0–20	6.09
0–1	0.08	0–9	1.68	0	0	0–5	0.46	0–6	0.46	0–26	6.55
0–1	0.08	0–10	1.76	0	0	0–5	0.46	0–5	0.39	0–31	6.94
0	0	0–10	1.76	0	0	0–5	0.46	0–1	0.08	0–32	7.02
0–1	0.08	0–10	1.84	0	0	0–5	0.46	0–1	0.16	0–33	7.18
0–1	0.08	0–10	1.92	0	0	0–5	0.46	0–1	0.16	0–34	7.34
0	0	0–10	1.92	0	0	0–5	0.46	0	0	0–34	7.34
0	0	0–10	1.92	0	0	0–5	0.46	0	0	0–34	7.34
0	0	0–10	1.92	0	0	0–5	0.46	0	0	0–34	7.34

mendations call for, the most abnormal one in the particular time period is used for scoring.

RADIOASSAY PROCEDURES—Although the radioassay tests, such as determination of Na^{24} activation in urine, blood, and whole body following neutron exposure, are dosimetry tests performed by the health physicist rather than clinical laboratory procedures, they are mentioned in Table XII, since they require the cooperation and judgment of the physician. If at all possible, the accomplishment of these procedures should be facilitated since knowledge of the physical exposure dose is a most valuable supplement to the clinical injury estimate. It may allow for early identification of the hyperresponsive patient and make clinical management easier thereby. Details of the dosimetry techniques are in a recent report[10] concerning radiation accident dosimetry.

SUBSEQUENT DIAGNOSTIC PROCEDURES—When

TABLE IX—INTEGRAL AND CUMULATIVE RANGE

	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Day	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0	0	0	0	0–1	0.25	0–1	0.25	0–1	0.25	0–1	0.25
2	0	0	0	0	0	0	0–1	0.25	0	0	0–1	0.25
3	0	0	0	0	0	0	0–1	0.25	0	0	0–1	0.25
6	0	0	0	0	0–2	0.50	0–2	0.75	0	0	0–1	0.25
9	0–1	0.13	0–1	0.13	0–2	0.75	0–3	1.50	0–1	0.13	0–1	0.38
12	0	0	0–1	0.13	0–2	1.00	0–5	2.50	0–1	0.13	0–2	0.51
15	0	0	0–1	0.13	0–2	0.75	1–6	3.25	0	0	0–2	0.51
18	0–1	0.13	0–1	0.26	0–1	0.50	2–7	3.75	0	0	0–2	0.51
21	0–1	0.50	0–3	0.76	0–2	0.88	2–8	4.63	0	0	0–2	0.51
24	0–1	0.50	0–4	1.26	0–2	1.13	3–10	5.76	0–2	0.38	0–2	0.89
27	0–2	0.25	0–6	1.51	0–3	1.63	3–13	7.39	0–4	1.13	0–6	2.02
30	0–1	0.25	0–6	1.76	1–4	2.25	4–17	9.64	0–4	1.63	0–10	3.65
33	0–3	0.88	0–9	2.64	1–3	2.38	6–20	12.02	0–4	2.13	1–13	5.78
36	0–3	0.88	0–12	3.52	1–3	2.38	8–23	14.40	0–4	2.25	1–16	8.03
40	0–3	1.00	0–15	4.52	1–3	1.88	9–25	16.28	0–3	1.50	1–19	9.53
44	0–3	1.13	0–18	5.65	0–2	1.25	9–27	17.53	0–2	0.75	1–20	10.28
48	0–2	0.75	0–20	6.40	0–2	0.63	9–27	18.16	0–2	0.50	1–20	10.78
60	0–2	0.63	0–21	7.03	0–1	0.13	9–27	18.29	0	0	1–20	10.78
75	0–2	0.63	0–22	7.66	0	0	9–27	18.29	0	0	1–20	10.78
90	0–2	0.25	0–22	7.91	0	0	9–27	18.29	0	0	1–20	10.78
105	0–1	0.13	0–22	8.04	0	0	9–27	18.29	0	0	1–20	10.78
120	0	0	0–22	8.04	0	0	9–27	18.29	0	0	1–20	10.78

TABLE X—INTEGRAL AND CUMULATIVE RANGE

	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Day	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0–1	0.80	0–1	0.80	0–1	0.20	0–1	0.20	0–2	0.40	0–2	0.40
2	0	0	0–1	0.80	1	1.00	0–2	1.20	2	2.00	0–4	2.40
3	0–1	0.40	0–2	1.20	1–3	2.00	2–3	3.20	0–2	0.60	0–6	3.00
6	0–1	0.40	0–3	1.60	1–3	2.00	3–6	5.20	0–3	0.80	0–9	3.80
9	0–1	0.40	0–4	2.00	0–3	2.00	5–9	7.20	1–2	1.20	1–10	5.00
12	0–1	0.60	0–5	2.60	0–4	2.20	5–13	9.40	0–4	1.20	1–10	6.20
15	0–1	0.60	0–6	3.20	0–3	2.00	5–16	11.40	0–2	0.80	1–11	7.00
18	0–1	0.60	0–7	3.80	0–3	2.00	5–19	13.40	0–3	1.20	1–12	8.20
21	0–1	0.60	0–8	4.40	1–3	2.20	6–22	15.60	0–3	1.00	1–13	9.20
24	0–2	1.00	0–10	5.40	2–4	3.00	10–25	18.60	0–4	2.00	1–17	11.20
27	0–2	1.20	0–12	6.60	2–4	3.40	13–29	22.00	1–4	3.20	2–20	14.40
30	1–2	1.75	4–14	8.35	3–4	3.75	21–33	25.75	0–4	3.00	2–21	17.40
33	1–3	2.00	7–16	10.35	3–4	3.75	25–37	29.50	3–4	3.75	6–25	21.15
36	1–2	1.75	8–18	12.10	2–4	3.00	28–41	32.50	0–4	2.50	10–29	23.65
40	1–2	1.50	10–20	13.60	0–4	2.25	30–45	34.75	0–4	2.00	13–33	25.65
44	1–2	1.75	12–22	15.35	0–4	2.00	30–49	36.75	0–3	1.50	14–36	27.15
48	1–2	1.25	15–24	16.60	0–3	1.25	31–52	38.00	0–2	0.50	14–38	27.65
60	1–2	1.25	16–26	17.85	0–3	0.75	31–55	38.75	0–2	0.50	14–40	28.15
75	1	1.00	17–27	18.85	0–1	0.25	31–56	39.00	0	0	14–40	28.15
90	0–1	0.50	17–28	19.35	0–2	1.50	33–58	40.50	0	0	14–40	28.15
105	0–1	0.50	17–29	19.85	0–2	1.00	35–60	41.50	0	0	14–40	28.15
120	0–1	0.25	17–30	20.10	0–2	1.00	36–62	42.50	0–1	0.25	14–41	28.40

the preliminary radiation injury group assignment of a given patient has been made, further diagnostic tests are designed to verify the assignment, to identify complications, and to aid in their management. Only a few Type B tests have been mentioned in Table XII. These are not intended to exclude others, but are merely the ones which seemed most useful in past cases and the ones for which early baseline values might be desired.

The few Type C procedures in Table XII are those used in some of the cases reviewed which seemed to be related to the extent of injury. Insufficient frequency of application prevent any definite opinion about their value as yet. Of course, many other procedures may also prove to be applicable to this type of clinical problem.

CLINICAL MANAGEMENT—As in the case of diagnostic procedures, a consideration of the

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP II

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–2	0.88	0–2	0.88	0	0	0	0	0–2	1.38	0–3	1.38
0–2	1.00	0–4	1.88	0	0	0	0	0–2	1.00	1–4	2.38
0–2	0.88	0–6	2.76	0	0	0	0	0–2	0.88	1–6	3.26
0–4	1.88	0–8	4.64	0	0	0	0	0–4	2.38	2–10	5.64
0–3	1.38	1–10	6.02	0	0	0	0	0–5	2.39	3–13	8.03
0–3	1.25	2–12	7.27	0–1	0.25	0–1	0.25	1–4	2.63	4–15	10.66
0–3	0.75	2–15	8.02	0–1	0.13	0–2	0.38	0–4	1.63	10–19	12.29
0–3	0.75	2–18	8.77	0–2	0.88	0–4	1.26	0–5	2.26	11–24	14.55
0–3	1.38	2–21	10.15	1–4	1.88	1–6	3.14	2–7	4.64	15–24	19.19
0–2	1.13	2–21	11.28	1–4	2.50	2–9	5.64	2–9	5.64	19–38	24.83
0–2	0.63	2–23	11.91	2–4	2.63	4–12	8.27	2–13	6.27	21–51	31.10
0–2	0.75	2–25	13.03	1–4	2.50	6–15	10.77	2–14	7.38	24–47	38.48
0–2	1.00	2–27	13.66	1–4	2.50	8–18	13.27	2–13	8.89	27–60	47.37
0–2	0.63	2–29	14.29	1–3	1.88	9–20	15.15	2–13	8.02	29–89	55.39
0–2	0.25	2–31	14.54	0–3	1.13	10–21	16.28	2–11	5.76	31–78	61.15
0–2	0.38	2–33	14.92	0–2	0.25	10–21	16.53	0–8	3.76	31–106	64.91
0–2	0.25	2–35	15.17	0–2	0.25	10–21	16.78	0–8	2.38	44–110	67.29
0–2	0.25	2–35	15.42	0–1	0.13	10–21	16.91	0–2	1.14	44–86	68.43
0	0	2–35	15.42	0	0	10–21	16.91	0–2	0.63	44–112	69.06
0–4	0.50	2–35	15.92	0	0	10–21	16.91	0–4	0.75	31–112	69.81
0–1	0.38	2–35	16.30	0	0	10–21	16.91	0–1	0.51	31–112	70.32
0–2	0.25	2–35	16.55	0	0	10–21	16.91	0–2	0.25	31–112	70.57

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP III

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–1	0.20	0–1	0.20	0	0	0	0	1–4	1.60	1–4	1.60
3	3.00	0–4	3.20	0	0	0	0	6	6.00	1–10	7.60
2–4	3.40	2–8	6.60	0	0	0	0	4–9	6.40	5–17	14.00
3–4	3.40	6–11	10.00	0–2	0.40	0–2	0.40	5–9	7.00	10–25	21.00
2–4	2.80	8–15	12.80	0–2	0.60	0–3	1.00	5–9	7.00	15–32	28.00
1–4	2.00	9–19	14.80	0–2	0.60	0–4	1.60	4–11	6.60	20–38	34.60
1–3	2.00	10–21	16.80	0–2	1.00	0–6	2.60	4–9	6.40	24–43	41.00
1–4	1.80	13–22	18.60	0–2	0.80	0–7	3.40	2–13	6.40	27–56	47.40
1–4	2.00	14–23	20.60	2–3	2.20	2–10	5.60	5–11	8.00	32–60	55.40
2–4	3.00	16–26	23.60	2–4	2.20	4–13	7.80	7–16	11.20	52–79	66.60
0–4	3.00	16–30	26.60	2–4	2.80	7–16	10.60	12–17	13.60	46–96	80.20
1–4	3.00	17–32	29.60	2–3	2.75	10–19	13.35	9–17	14.25	55–113	94.45
0–4	2.25	21–36	31.85	2–3	2.25	12–21	15.60	10–17	14.00	72–130	108.45
0–4	2.00	22–40	33.85	0–2	1.25	13–21	16.85	4–16	10.50	84–146	118.95
0–4	1.25	22–44	35.10	0–2	1.00	14–21	17.85	2–16	8.00	93–162	126.95
0–3	0.75	22–47	35.85	0–2	0.50	14–22	18.35	1–14	6.50	100–176	133.45
0–3	1.25	22–48	37.10	0–1	0.50	14–23	18.85	3–9	4.75	103–185	138.20
1–3	1.75	24–51	38.85	0–1	0.25	14–23	19.10	2–10	4.50	105–195	142.70
0–1	0.50	25–52	39.35	0	0	14–23	19.10	1–3	1.75	106–198	144.45
1–3	2.00	28–54	41.35	0–1	0.50	15–24	19.60	1–6	4.50	112–204	148.95
1–4	2.25	29–58	43.60	0	0	15–24	19.60	1–7	3.75	115–211	152.70
1–3	1.50	30–61	45.10	0–1	0.25	15–25	19.85	1–8	3.25	116–219	155.95

TABLE XI—INTEGRAL AND CUMULATIVE RANGE

	Erythrocytes				Leucocytes				Neutrophils			
	Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Day	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
1	0–1	0.50	0–1	0.50	0–1	0.50	0–1	0.50	0–2	1.00	0–2	1.00
2	0	0	0–1	0.50	1	1.00	0–2	1.50	2	2.00	0–4	3.00
3	0	0	0–1	0.50	1–2	1.50	1–4	3.00	0–4	2.00	0–8	5.00
6	0	0	0–1	0.50	2–4	3.00	3–8	6.00	0–4	2.00	0–12	7.00
9	0	0	0–1	0.50	3–4	3.50	6–12	9.50	3–4	3.50	3–16	10.50
12	0	0	1	0.50	4	4.00	10	13.50	3	3.00	6	13.50
15	0	0	1	0.50	2	2.00	12	15.50	0	0	6	13.50
18	1	1.00	2	1.50	3	3.00	15	18.50	1	1.00	7	14.50
21	1	1.00	3	2.50	4	4.00	19	22.50	4	4.00	11	18.50
24	1	1.00	4	3.50	3	3.00	22	25.50	3	3.00	14	21.50
27	1	1.00	5	4.50	4	4.00	26	29.50	4	4.00	18	25.50
30	1	1.00	6	5.50	1	1.00	27	30.50	0	0	18	25.50

INTEGRAL AND CUMULATIVE RANGE AND

1	2.00	2.00	3.00	3.00	4.00	4.00
2	0	2.00	3.00	6.00	4.00	8.00

choice and results of past methods of therapy helps to shape the present recommendations. The types of agents employed in the accidents reported herein are listed in Table XIII. It will be seen that only in cases which fall into Group II or above has specific treatment appeared necessary. In general, since the means to reverse the basic cellular mechanisms which underlie radiation effect are not yet at hand, the clinical approach has been supportive, with specific therapy being reserved for symptomatic indications.

As has already been indicated, it is desirable for all cases with a probability of significant acute injurious radiation overexposure to be hospitalized for close observation. The accomplishment of the preliminary estimation of clinical radiation injury as described in the preceding section on diagnostic procedures should indicate within 72 hours those cases falling into Group II or above. These should be kept hospitalized. The others can be reassured of their favorable prognosis and released from inpatient care when asymptomatic.

GROUP I—These patients can be followed as outpatients, using the previously suggested tests. There is no specific medical contraindication to a return to work as soon as dosimetry, clinical symptoms and findings, and laboratory data have established the low level of overexposure. Considerations of public opinion, medicolegal sequelae, and the like, doubtless have played a role in the more conservative prescription of a rest period of varying length which has been utilized in several cases within Group I. It is definitely recommended that subsequent work be in a capacity in which further radiation overexposure is unlikely.

GROUP II—Patients in this group will exhibit transient nausea and vomiting which will probably not require more than the administration of antiemetic agents, if that. There is no definitive therapeutic procedure for radiation epilation other than reassurance concerning its impermanence in this group.

Complications of the existing bone marrow damage, such as anemia, infection, and evidences of bleeding, have been mild when present at all in Group II. It is therefore considered advisable to adopt a conservative attitude of watchful waiting, with the means for vigorous and definitive treatment available if and when needed. Thus, blood and perhaps platelet transfusions, antibiotics, and the like should be ready in reserve. An attempt to reduce the likelihood of infections by emphasis on personal hygiene and the use of aseptic isolation methods may well be warranted.

The mechanism of the observed weakness and fatigue of these patients is not clear, and therefore no specific therapy can be recommended at this time. Rest is indicated until symptoms and major laboratory abnormalities subside. The opportunity for future occupational radiation exposure should be minimal.

GROUP III—It is the therapeutic management of patients in Group III that presents the most challenging opportunity to alter an otherwise unfavorable prognosis. In this group one can expect to deal with the major complications of serious bone marrow damage, some gastrointestinal injury, and secondary renal and cardiovascular problems.

Prompt bed rest, bland diet, good nursing care, and a realistic but generally reassuring appraisal of the medical situation are indicated

AND MEAN OF BLOOD COUNT PROFILE SCORES—GROUP IV

Lymphocytes				Platelets				Total			
Integral		Cumulative		Integral		Cumulative		Integral		Cumulative	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
0–2	1.00	0–2	1.00	0	0	0	0	1–5	3.00	1–5	3.00
4	4.00	0–6	5.00	0	0	0	0	7	7.00	1–12	10.00
4	4.00	4–10	9.00	0	0	0	0	5–10	7.50	6–22	17.50
4	4.00	8–14	13.00	2	2.00	2	2.00	8–14	11.00	14–36	28.50
3–4	3.50	11–18	16.50	2–4	3.00	4–6	5.00	11–16	13.50	25–52	42.00
4	4.00	15	20.50	3	3.00	7	8.00	14	14.00	39	56.00
4	4.00	19	24.50	3	3.00	10	11.00	9	9.00	48	65.00
3	3.00	22	27.50	4	4.00	14	15.00	11	11.00	59	76.00
3	3.00	25	30.50	4	4.00	18	19.00	15	15.00	74	91.00
1	1.00	26	31.50	4	4.00	22	23.00	11	11.00	85	102.00
4	4.00	30	35.50	3	3.00	25	25.00	16	16.00	101	118.00
4	4.00	34	39.50	0	0	25	26.00	6	6.00	107	124.00

MEAN OF BLOOD COUNT PROFILE SCORES—GROUP V

	4.00		4.00						13.00		13.00
	4.00		8.00						11.00		24.00

as soon as dosimetry, symptomatology and hematological "profile" makes classification in Group III apparent.

Antiemetics are indicated for severe and prolonged nausea and vomiting in the initial phase or later. Intravenous feeding may be necessary as well, to maintain fluid and caloric balance in the early stage or in the later course when gastrointestinal symptoms may recur. The maintenance of acid-base and electrolyte balance should be attempted also, with frequent serum pH, acid-base, and electrolyte studies as a guide.

When increasing evidence of depression of bone marrow function ensues toward the second and third weeks after exposure, certain precautions are indicated. To reduce infections, an effort to minimize bacterial exposure should be attempted, utilizing isolation and aseptic techniques in contacts with the patients. Although prophylactic antibiotics have been employed in many instances, real proof of their value for this purpose is not too clearcut. There are indications that such use may have blunted their effectiveness in subsequent infections during the course. Recently, it has been suggested[27] that penicillin and aureomycin be used orally, starting at five to seven days after exposure in doses of 100,000 units every four hours and 250 mg every six hours respectively. Bacteriocidal antibiotics in parenteral form should be reserved for therapeutic use in high dosage when infections of overt or even occult nature occur. These may be suggested by symptoms, by fever, or simply by a sharp rise in a previously low sedimentation rate, despite the absence of any resultant leucocytosis. Bacterial sensitivity studies should be performed and their results used as a therapeutic guide, if possible.

Hemorrhagic phenomena are difficult to treat by any conventional means. Platelet transfusions have been tried with some possible temporary benefit resulting.[19] Anemia, which develops insidiously, will respond to conventional transfusion therapy. This should be used only when a clinically significant fall in red cell volume has developed.

A new form of therapy may be utilized to treat severe pancytopenia accompanied by distinct clinical sequelae, such as uncontrollable infection or bleeding, with a clearly grave prognosis. This is the performance of bone marrow transplantation using cells from a homologous donor, matching in sex, and in major, and most minor blood subgroups. The time for successful performance of this procedure had previously been considered to be limited to a few days after radiation exposure. Now, the recent, apparently helpful, use of such a transplantation procedure in the Yugoslavian accident patients[22] about a month after exposure suggests that the decision concerning its use can await the unfolding of the clinical course. This delay removes the necessity to base such action on the preliminary physical dosimetry and early, fragmentary data concerning the extent of radiation injury.

Very little is known as yet about the utility or even desirability of bone marrow transplantation in man. In the treated Yugoslavian patients, a prompt rise to a peak occurred in the level of granulocytes, platelets, and reticulocytes before such improvement was found in a lower dose patient recovering spontaneously. Also, the pattern of platelet response was some-

TABLE XII—RECOMMENDED DIAGNOSTIC PROCEDURES FOR CLINICAL MANAGEMENT OF RADIATION INJURY

Group		I-II-III-IV			I		II		III		IV	V
Procedure	Time (d)	1	2	3	STT	STT	18-48	STT	4-48	STT	4	1
TYPE A												
History												
Symptoms, Signs	onset, duration	x	x	x	x	x	D	x	D	x	D	D
Past Medical		x										
Physical Examination												
General		x					d21	3 mo⁻	d15–30	3 mo⁻	d6	D
Body weight		x			x	x	D	x	D	x	D	D
Urinary output		x	x	x		x	D		D		D	6 hr
Laboratory Tests												
Hematology												
Hematocrit		x	x	x	x	x	D	x	STT	x	D	6 hr
Leukocytes		x	x	x	x	x	D	x	D	x	D	6 hr
Differential Count		x	x	x	x	x	D	x	D	x	D	6 hr
Calculation of Total Neut. and Lymph.		x	x	x	x	x	D	x	D	x	D	6 hr
Platelets		x	x	x	x	x	D	x	STT	x	D	6 hr
Bone Marrow Aspiration					d30	14d	14d	mo6	14d	mo6	7d	d1
Radioassay												
Blood Na^{24}		x	x									
Whole Body Counting		x	x									
TYPE B												
Laboratory Tests												
Hematology												
Sedimentation Rate		x	x	x	x	x	D	x	D	x	D	6 hr
Reticulocytes		x	x	x	x	x	D	x	STT	x	D	6 hr
Bleeding, Clotting	Times	x					STT		STT	–75d	3d	6 hr
Biochemistry												
Blood												
NPN		x	prn	prn					prn		STT	6 hr
Sodium		x	prn	prn					prn		prn	d1
Chloride		x	prn	prn					prn		prn	d1
Potassium		x	prn	prn					prn		prn	d1
pH or Co_2		x	prn	prn					prn		prn	d1
Urine												
Routine analysis		x	x	x		x	D	x	D	x	D	6 hr
Stool												
Occult blood		x					D		d12⁺		D	All
Ophthalmology												
Slit lamp				x	6mo⁻			6mo⁺		6mo⁺		
TYPE C												
Biochemistry												
Serum bilirubin		x	x	x		x	STT		STT	–30d	D	6 hr
Urine BAIBA		x			–30d	x	D		D		D	D

STT Standard Testing Times—6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 40, 44, 48, 60, 75, 90, 105, 120 days 6 mo., 1 yr. and annually.

Recommended frequency of time of performance:

- x —— at times indicated in column heading
- d —— daily during time indicated in column heading
- nd —— frequency in days
- –dn —— up to and including day at times indicated in column heading
- dn⁺ —— on and after day at times indicated in column heading
- dn —— specific day recommended
- n —— all time after day specified
- prn —— as indicated by clinical course

TABLE XIII—SUMMARY OF THERAPEUTICS EMPLOYED IN GROUPS II, III, IV, AND V

	Group II								Group III						Group IV		Group V
Therapy	LA4	R1	R2	OR1	OR2	OR3	OR4	OR5	Y6	LA1	Y2	Y3	Y4	Y5	LA3	Y1	LAII
Sedation	....	....	....	....	....	X	....	....	....	....	....	....	....	....	....	....	X
Analgesics	....	X	....	....	....	X	....	....	....	X	....	....	....	....	X	....	X
Antiemetics	....	....	....	X	....	X	X	X	....	....	....	....	....	....	....	....	....
Antispasmodics	....	X	....	....	....	X	....	....	....	....	....	....	....	....	....	....	....
Parenteral fluids	X	....	....	....	....	....	....	....	....	X	....	....	....	....	X	....	X
Electrolytes	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Whole blood	X	X	X	....	....	....	....	....	X	X	X	X	X	X	X	X	....
Plasma	X	....	....	....	....	....	....	....	....	....	....	....	....	....	X	....	X
Platelets	....	....	....	....	....	....	....	....	....	....	X	X	....	....	....	X	....
Bone marrow	....	....	....	....	....	....	....	....	....	....	X	X	X	X	....	X	....
Antibiotics	X	X	X	X	....	....	X	....	X	X	X	X	X	X	X	X	....
Vasoconstrictors	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	....	X
Vitamins	....	X	X	....	....	....	....	....	X	X	X	X	X	X	....	X	....
Hematinics	....	X	X	....	....	....	....	....	....	....	....	....	....	....	....	....	....
Miscellaneous	....	X	X	....	....	....	....	....	....	X	....	....	....	....	....	X	....

X Therapy used one or more times.

what different. Furthermore, red cell agglutination tests indicated a phase of increase in the number of donor cells during the time when transfused cells would have been decreasing. However, there may be a relative and gradual recession of the hematological picture subsequently at a time when the late "immune disease" which characterizes graft rejection in lower mammals might be expected.

It may prove that the donor marrow served as a temporarily functioning bridge over the hiatus in the patients' blood formation process. What the over-all value of the transplant procedure will be cannot yet be stated. It should be reserved as a desperate measure against overwhelming clinical odds for seriously ill patients in Group III and above until more data become available.

In the more seriously affected patients in Group III, occurrence of rather severe gastrointestinal symptomatology, including partial intestinal obstruction, may take place. A bland diet in the acute illness phase may be helpful in minimizing such difficulties.

GROUP IV—The patients in this range have run a course similar to those in the upper end of Group III but telescoped into a shorter time period, and with a fatal outcome. Gastrointestinal difficulties require the major therapeutic effort before hematological disturbances reach full fruition. Vigorous treatment, including tubal gastrointestinal decompression, fluid replacement with correction of electrolyte and caloric deficits, the use of antiemetics, antihypotensive agents, antibiotics, and bone marrow transplantation, are advocated in this situation.

Secondary cardiovascular and renal failure may further complicate this grave clinical state. Response to hemodialysis in one such instance was poor. Detailed biological data collection is particularly indicated in these difficult cases if present-day therapeutic inadequacy is to be altered in the future.

GROUP V—The one case in this group showed the evidence of the experimentally anticipated central nervous system injury associated with very high radiation dose. Palliation of the accompanying hypotension and gastrointestinal symptoms was carried out. No specific recommendations are yet available for this situation, other than supportive therapy.

LATE SEQUELAE—The only late sequela of radiation overexposure in the accident cases reported herein has been the development of bilateral cataracts. There is no known prophylaxis against this occurrence, but if the usual spontaneous regression of the radiation cataract is inadequate, the ordinary surgical procedure for its removal is satisfactory.

No other long-term effects can be anticipated specifically in any given case, although the general statistical probability of leukemogenesis, carcinogenesis, or genetic mutation may be slightly enhanced. There are no such findings reported in any of these cases.

Conclusions

The general medical findings in the radiation accident patients reviewed in this report are not novel. They correspond with those reported in a number of other situations in which humans have been exposed to significant whole-body radiation overexposure. However, these particular findings stem from the types of accidents which are of special interest to an increasing number of physicians now coming into contact with the fast-growing field of nuclear technology. For this reason, conclusions drawn from this series may be especially useful.

It is rather reassuring to find that, despite the disturbing physical complexity of nuclear criticality accidents, the key procedures for clinical evaluation of resultant injury are such familiar ones as a detailed medical history, thorough physical examinations, and accurate blood counts. The additional support provided by improvements in radiation dosimetry and modern clinical laboratory procedures is, of course, very helpful as well.

In the therapy of such patients also, good medical management, firmly based on an understanding of the pathophysiology of the acute radiation syndrome, does not really differ from the treatment of less modern maladies. The development of bone marrow transplantation as a possible specific form of treatment for this syndrome does provide, however, a somewhat specialized therapeutic procedure.

Concerning the relative value of physical dose measurements and biological signs of injury as aids in the care of human radiation overexposure, the nature of the exposure incident is most important. What is suited to the triage of victims of a nuclear warfare catastrophe is not necessarily appropriate for the industrial accident victim. The utilization of precise clinical observations and frequent laboratory tests as advocated herein, with calculation of the injury profile score, may not be feasible under other circumstances. However, it is considered to be of particular value, especially when supplemented with good mixed radiation dosimetry, in medical management of the accidents of nuclear technology.

Summary

In order to familiarize the medical profession with current concepts about the diagnosis and management of a rare but increasingly frequent clinical entity, the acute radiation syndrome, all pertinent radiation accident cases have been reviewed. Circumstances; dosimetry; clinical signs, symptoms, and course; laboratory findings; and therapy are considered. On the basis of these data, recommendations for diagnosis and treatment are made to aid in clinical management, to facilitate the development of improved diagnostic procedures, and to increase the fund of biomedical data from which stems our understanding of human radiation injury.

Acknowledgments

Sincere appreciation is expressed to many individuals and groups in many countries who freely supplied unpublished information, advice, aid, recommendations, and encouragement to the authors. Among these are K. Z. Morgan, G. S. Hurst, and R. H. Ritchie, the Health Physics Division, Oak Ridge National Laboratory; W. T. Ham Jr., Medical College of Virginia; M. Brucer and G. Andrews, Oak Ridge Institute of Nuclear Studies; T. Shipman, Los Alamos Scientific Laboratory; E. Saenger, University of Cincinnati; R. Latarjet, Institut du Radium, Paris; G. Mathé, Hôpital Herold (Association Claude Bernard) et Hôpital Curie, Paris; P. S. Henshaw, U. S. Atomic Energy Commission; C. G. Stewart, Atomic Energy of Canada, Ltd.; R. Wégria, St. Louis University, and A. G. Kammer, University of Pittsburgh.

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Toxicology of Diisocyanates

Rex H. Wilson, M.D., and George L. Wilson, Akron, Ohio

THE RUBBER industry has developed an interest in a new class of polymers known as the polyurethanes. In the hands of the resourceful chemist, products such as adhesives, rigid and elastic foams, plastics, and man-made rubber can be fashioned with these highly versatile polymers.

One of the raw materials used in the manufacture of the polyurethanes is a group of chemicals known as diisocyanates. These chemicals known to the chemist for many years, have suddenly zoomed to importance commercially. Several of them have been adapted to industrial applications. Among these are toluene diisocyanate (TDI), *p*-phenylene diisocyanate (pPDI), and methylene bis (4-phenyl isocyanate) (MDI). TDI may be used either as the 2,4 or 2,6 isomer or a mixture of the two. Another diisocyanate which has been scrutinized by the industrial researcher is 1,5-napthalene diisocyanate (NDI).

In general, all the isocyanates exhibit the rather unusual characteristic of a low oral toxicity with a high chronic inhalation toxicity. They all have the potential of producing asthma-like symptoms.[1]

Much of the toxicological information available is based on animal exposure to and industrial use of TDI. Zapp[2] investigated the toxicity of toluene 2,4-diisocyanate and concluded that the acute toxicity of TDI is not high but that it is a powerful irritant of the eyes, skin, gastrointestinal tract and respiratory tract, and that, in addition, there is the definite possibility of sensitization resulting in asthmatic attacks.

The acute oral toxicity of TDI was investigated by the administration of the undiluted material by stomach tube to rats. Pathology examination revealed a corrosive action on the stomach as well as a possible toxic effect on the liver. The approximate lethal dose was 5,800 mg/kg. Subacute oral tests, wherein rats received 1,500 mg/kg per day, resulted in the death of three of six animals with 10 treatments. Pathological examination again revealed injury to the gastrointestinal tract and liver. Zapp states that these results suggested the possibility of cumulative effects.

Acute skin absorption tests on rabbits produced severe local irritation but failed to kill or produce anatomical injury to internal organs. A 10% solution in dimethyl phthalate irritated the intact skin of guinea pigs. It was also possible to produce allergic skin sensitization in guinea pigs.

The application of TDI to the rabbit eye caused irritation of the eyelids and mild damage to the corneal epithelium unless the eyes were promptly and thoroughly flushed with water.

Acute inhalation studies revealed that 600 ppm for six hours was lethal to rats but 60 ppm was not. Animals which died showed acute pulmonary congestion and edema.

Subacute inhalation studies with rats, guinea pigs, and rabbits showed that six exposures to 9 ppm killed three of six rats but no guinea pigs or rabbits. All survivors had bronchitis and minimal bronchial pneumonia, whereas the rats that died showed bronchitis and definite bronchial pneumonia.

Additional subacute inhalation tests performed by Zapp revealed the following facts:

1. Ten six-hour exposures to 1 to 2 ppm of TDI produced no injury to rats, but after 30 six-hour exposures, microscopic evidence of tracheobronchitis was detected.
2. Five rats survived 79 six-hour exposures to 1.5 ppm, with four of them showing bronchitis of varying degrees when killed.
3. Guinea pigs killed after 23 to 79 six-hour exposures to 1.5 ppm all showed bronchitis with varying degrees of bronchial pneumonia.
4. One rabbit died after three, and one after five, exposures to 1.5 ppm. Others, surviving

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19 to 71 exposures, showed bronchitis, and in one case, slight pulmonary edema.

5. Four dogs reacted to 1.5 ppm with lacrimation, coughing, restlessness, and spitting-up of frothy material. Because of these reactions, exposure was limited to periods of 30 minutes to two hours daily, and the animals were exposed 35 to 37 times. No consistent objective signs of anatomical injury could be detected during exposure. When killed after the last exposure, all dogs showed mild congestion and inflammation of the trachea and large bronchi, with some of the bronchial branches having thick mucous plugs.

These findings agree generally with those of other investigators. Fuchs and Valade[3] reported that a mixture of 2,4 and 2,6-toluene diisocyanates caused respiratory irritation. They also noted an asthmatic reaction in humans which Zapp did not observe in animals, but which indicates an inhalation sensitization in man. Others, in both published and unpublished reports, have mentioned the occurrence of an asthmatic-type reaction upon only slight exposure after previous severe exposures.

The threshold limit value for toluene 2-4 diisocyanate is established at 0.1 ppm.[4, 5] This low atmospheric concentration for prolonged human exposure indicates the highly irritating nature of these vapors.

A human sensitivity test involving 24 persons was made using toluene diisocyanate vapors.[6] Fifty per cent of the subjects reported the least detectable odor was 0.4 ppm. Irritation of the nose and throat occurred at 0.5 ppm, and an appreciable odor was noted at 0.8 ppm. All these concentrations are well above the threshold limit value. This emphasizes the necessity for quantitative air evaluation instead of dependence upon human response.

To avoid contamination of the workroom requires all of the acumen of a highly trained industrial hygienist. Well-designed equipment and good local exhaust ventilation are essential if the low level of 0.1 ppm is to be maintained. Frequent air sampling must be performed. The analytical method of Marcali[7] is satisfactory for this purpose and may be adapted to other diisocyanates.

Care should be used to prevent contact between TDI and water or water vapor. Neither water nor acids should be added in a confined space, as carbon dioxide gas is evolved and the resulting pressure may rupture the container. Strongly alkaline materials, such as aqueous sodium hydroxide and soda ash, will react violently. Adequate floor drainage, hoses, buckets, and mops should be available in work areas where spills can occur. A good decontaminant is an aqueous 5% ammonia solution containing 10% isopropyl alcohol.[6]

In case of eye contact, the eye should be irrigated immediately with large amounts of water, preferably at an eye fountain, for 15 minutes as a first-aid measure. The patient should then be referred to a physician for examination and further treatment. If the material is spilled on the body, the contaminated clothing should be removed and the body washed first with 30% isopropyl alcohol (rubbing alcohol) and then with soap and water.[6] Safety showers are advisable in work areas. Some darkening and hardening of the skin of workers repeatedly exposed to diisocyanates has been observed.[8]

Close medical supervision of all exposed persons is necessary. A preplacement examination, which includes a chest roentgenogram, should be given to every one prior to assignment involving potential exposure to isocyanates.[1] Individuals presenting abnormal pulmonary findings or histories of respiratory allergies should not be exposed.

Persons presenting symptoms such as irritation of the nose, throat, or eyes, coughing, or asthmatic-like symptoms, should be placed under the care of a physician and further exposure discontinued.

Periodic physical examinations of exposed persons should be made, with emphasis on evaluation of the respiratory tract. This should include roentgenogram of the chest. If abnormalities are noted, particularly the presence of a peribronchial infiltration, the person should be removed from exposure.

As a general rule, persons removed from exposure because of clinical evidence of positive physical changes due to diisocyanates should never be permitted to be exposed again. There are some exceptions to this rule. Occasionally one encounters a person who has mucous membrane irritation at the beginning of exposure and then has no further symptoms. These individuals may continue to work under observation.

The treatment of exposure to diisocyanates is entirely symptomatic.

Summary

1. Diisocyanates in general are highly irritating to the respiratory tract and may produce asthma-like symptoms.

2. The threshold limit value is 0.1 ppm.

3. Good handling practices and excellent local exhaust ventilation are necessary if they are to be processed safely.

4. Care should be used to keep these materials off the skin and out of the eyes.

5. Accidental contact with water, acids and alkalies must be prevented.

6. Close medical supervision of all exposed persons with particular attention to the respiratory tract is necessary.

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Group Disability Insurance —Abuse and Control

Robert W. Butler, M.D., Waterbury, Connecticut

THE average practitioner in an industrial community in the United States is making an indirect contribution to an abuse which may be costing American industry upwards of $150,000,000 annually. This figure is an estimation which may be low, but points up the magnitude of a problem which has not been apparent to the individual physician who meets it in his practice only a few times each year. The estimate is based upon a study of the problem in two different types of industry in two different states, and also on the premise that human nature in Portland, Maine, is not vastly different from that in Portland, Oregon.

The group insurance plan for the income protection of workers disabled by off-the-job illnesses and accidents has had a tremendous growth in the past several years. Various types of this eminently desirable coverage are presently effective, but practically all are subject to the abuse with which this paper treats.

My interest in this matter dates back to the months of September and October, 1946. At this time, an insurance plan which provided disability payments for a total of 13 weeks for each nonoccupational illness or injury had been in effect for approximately two years. We were impressed during these two months by the number of women returning to work after absences of 11 to 14 weeks. Some of these absences followed operative procedures normally requiring relatively short periods of convalescence, and others were ascribed to minor medical conditions. Subsequent checking of the figures showed that the cost of the program for that year was about 115% of the premium. It was perfectly apparent that abuse existed and further investigation as to causes and groups responsible merely confirmed our suspicions—a high percentage of the abuse occurred during the summer months and was largely confined to women whose income from the job merely augmented and was not essential to the family livelihood. Much of this group was made up of married women between the ages of 25 and 45, whose children were home from school for the summer. It was interesting to note also that the general community health (or illness) curve and that of the insured group were similar only during the winter months. During June, July, and August, the curve was reversed by the insured group which showed an absentee incidence somewhat higher than that of January, February, and March.

In 1951, a study was made of the group accident and health experience in another company of similar size whose policy provided coverage for 26 weeks. This investigation covered closed cases which represented the experience of the first quarter of that year. We were interested primarily not in the total of 910 paid weeks lost, but rather in the total of 176 excess weeks paid which represented our estimate of the abuse.

Determination of abuse is obviously difficult, especially when it is based only upon information contained on claim and medical forms. Our procedure for estimating abuse in each case was based on several factors: first, the attending physician's diagnosis and his estimate of disability; second, our own knowledge of the average duration of disability for a given operation, illness, or accident. "Average duration of disability" is not inflexible, since it should take into consideration among other things, the factors of age, prior disabilities, and the physical and mental demands of the job to which the employee will return. All of

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these elements were considered in our estimates, using as a base line the following disability averages for several frequently encountered conditions:

Appendectomy	4-5 weeks
Cholecystectomy	4-6 weeks
Colles Fracture	6-8 weeks
Dilatation and Curettage	1-2 weeks
Hemorrhoidectomy	2-3 weeks
Herniorrhaphy	4-5 weeks
Hysterectomy	5-6 weeks
Perineorrhaphy	5-6 weeks
Pneumonia	4-6 weeks
"Rest Cures"	3-4 weeks
Tonsillectomy	1-2 weeks
"Virus Infection"	2-4 weeks

Finally, certain additions to compensate for complications not anticipated in the orginal medical report were made; and to accomplish this, one week was added to short-term illnesses and two weeks to long-term illnesses, after which it was considered that time was being lost in excess. Short-term illnesses were arbitrarily taken to be those which normally produce disability of two to four weeks; long-term illnesses those of six or more weeks. While additions of this sort might not have been adequate in individual cases, they represented an aggregate total of 255 weeks in the series under consideration; or approximately 28% more total time than should have been lost had no unforeseen complications developed. It was then felt that the resulting figures would produce an extremely conservative estimate of the actual abuse.

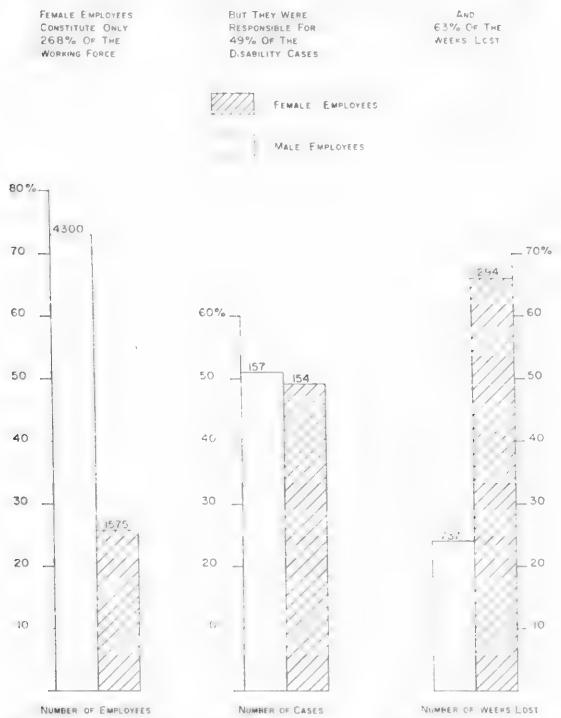

Fig. 1.—Group accident and sickness experience: study of 311 cases, June through September, 1951, causing 2031 weeks lost.

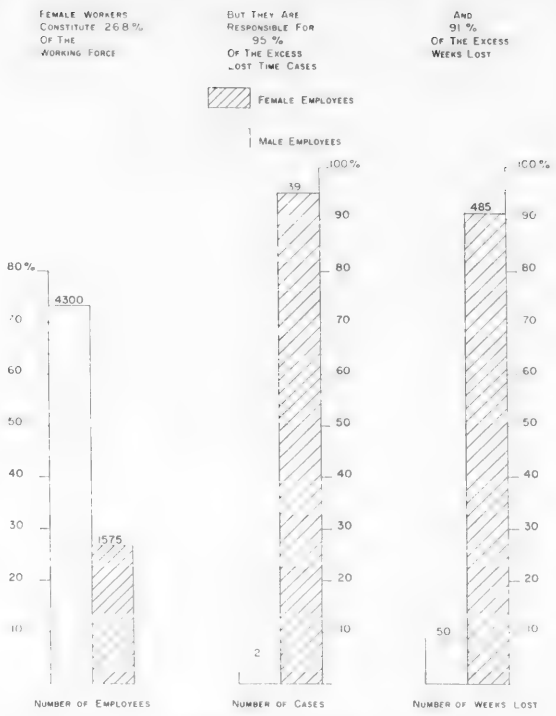

Fig. 2.—Study of 41 consecutive cases (four month period) having undue or excessive loss of time.

This survey showed a plant census of approximately one-third as many females as males, a total number of female claims approximately equal to the total number of male claims, and twice as many "female weeks" lost as "male." Of 274 cases, 34 lost a total of 176 weeks in excess, and of these 176, female employees lost 130 weeks. On investigation of all claims, those from married women aged 20 to 50 approached 75% of the unnecessary lost weeks, but only 8% of the total cases.

Subsequently, a second survey was made covering the months of June through September, 1951, known from previous experience to be the months of greatest abuse. It was interesting to note that the results were prognosticated to with 15% before the records were reviewed. As seen from Figure 1, the percentages by sex in total census, number of cases, and number of weeks lost are similar to those in the earlier study.

An analysis of the experience showed that of the total of 311 cases in this series, 41 were in excess for a total of 535 weeks. Of these

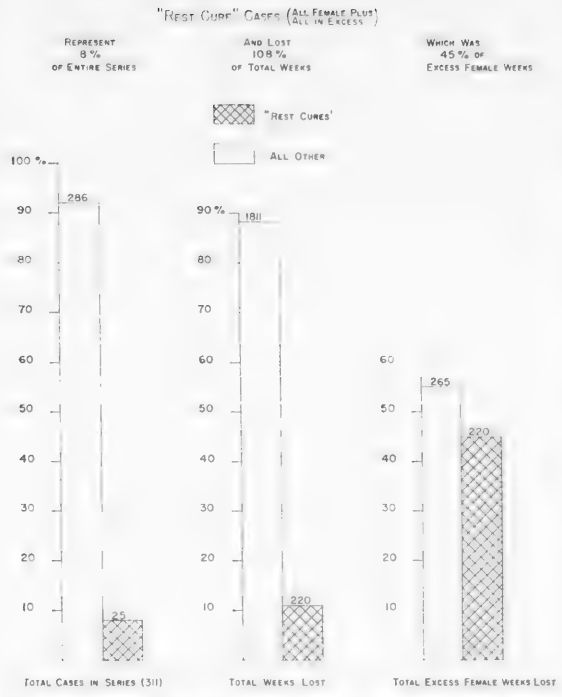

Fig. 3.—Study of consecutive cases (four month period) having undue or excessive loss of time.

excess weeks, 485 were lost by women employees and 50 by men. Figure 2 illustrates an analysis of these cases., in all of which an excess of six weeks' time was lost from work—39 of these were among females who lost a total of 394 weeks and 2 among males who lost 26 weeks. Incidentally, 23 of the 26 "male weeks" lost in excess were the result of one case of epidermophytosis involving the feet only, in which instance many unnecessary weeks apparently were to be attributed to error or poor control.

For lack of a more descriptive term, we have included a large number of much-abused diagnoses in the term "Rest Cures." These include neurocirculatory asthenia, hypotension, neurasthenia, secondary anemia, asthenia universalis, menopausal syndrome, and nervous exhaustion —among others. The proportion of these among all excess time lost cases in the series is illustrated in Figure 3.

We have thus presented the figures for that period of the year when the experience is admittedly poorest. However, the abuse during these four months probably does not greatly exceed one-half of the total of such losses for the entire year. Furthermore, the actual dollar cost shown in Figure 4 represents cash payments only and would be increased many thousands of dollars by the addition of insurance handling charges and costs of absenteeism. A conservative estimate of the aggregate cost of this abuse to the plant whose experience has been described would exceed $70,000 for that year!

Industry appreciates full well, we believe, that the average woman who works eight hours a day in a factory and follows this with added hours of intensive housekeeping and caring for her family may require more than the usual two weeks' annual vacation provided by the employer. This study took that fact into consideration and the final figures were not influenced by it. No rest cases were considered excessive whose absences were four weeks or less.

The family physician finds himself in a peculiarly difficult and embarrassing position in the handling of these cases of obvious abuse. If a patient has recovered but refuses to return to work, and the doctor refuses to certify the continuing disability, the result is predictable. In many cases he will lose not one, but several patients, and be the subject of criticism which may be as damaging as it is unfair and unwarranted.

On the other hand, physicians are appreciative of the benefits accruing to themselves from various plans providing income as well as hospital and surgical expenses for the disabled employee. The shift percentagewise in

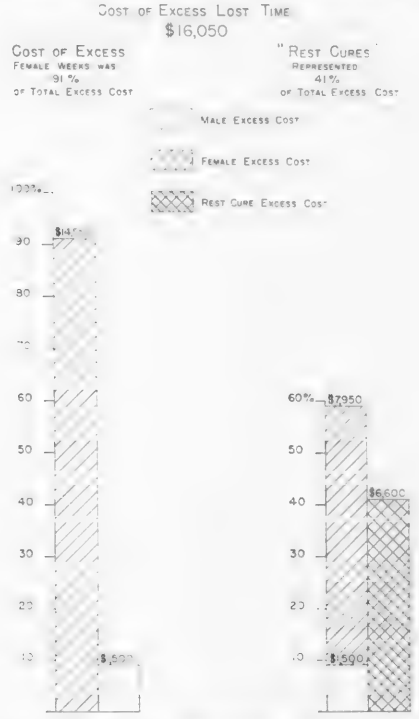

Fig. 4.—Study of 41 consecutive cases (four month period) having undue or excessive loss of time.

the number of private and public ward admissions to our hospitals in recent years offers ample testimony of this. The physician therefore has a stake not only in the program, but in its honest and equitable administration as well. Industry is not interested in curtailing benefits under the various plans, but it is awakening to the fact that something must be done to ease the excessive economic burden placed upon it by the steadily increasing abuse.

The most satisfactory solution to this problem is to be found by the individual physician and in local groups and societies; and solved it must be. It is intolerable that a very small percentage of employees in any industry should place in jeopardy a program which should be operative to the benefit of all.

It is probable that no single abuse control plan would be universally applicable, since each community has its own peculiar aspects of the problem. However, in a small community where the number of practicing physicians is not great, and personal contacts among representatives of industry, the insurance companies and all members of the profession are not difficult, a mere discussion and explanation of the problem may well be all that is required. In larger cities, this is obviously impracticable.

One plan which met with success in a city of 125,000 population and proved highly satisfactory to all concerned during a three-year period changed the loss in one plant from 115% to 85% of the premium during the first year, and from 85% to 74% during the second year—with no change in the basic premium rate. This was accomplished solely by an amelioration of the abuse. This plan is now effective in a second community of similar size and thus far has functioned very well.

The plan is based upon two changes in current practice. The first of these is a complete divorcement of the employee's claim form from that of the physician's report. Where these are found on opposite sides of the same form, the attending physician frequently finds himself in the unfortunate position of having to complete, at the patient's request, both the claim and the medical report; after which the patient returns the single form to the plant insurance office or to the insurance carrier. This provides the patient with both the diagnosis and the physician's estimate of the duration of disability—an undesirable situation for obvious reasons. This is eliminated by the use of two forms; one completed by the patient and returned to the employer, after which the medical report is mailed to the physician and returned directly by him.

The second change institutes the use of impartial examinations, when indicated, by a member of an examining board appointed not by industry or the insurance companies, but by the local medical society. The word "impartial" requires clarification. It refers not to the examination itself, but to the employee's impression of it. This panel of five members

ATTENDING PHYSICIAN'S REPORT

YOU WILL ASSIST YOUR PATIENT BY COMPLETING THIS FORM PROMPTLY

Since payments cannot be made until this form is returned

Patient's
1. Name ..... Age ..... Date First Examined ..... Where .....

2. Your complete diagnosis ..... (Please Print)

3. Is disability due to accident ..... (Yes or No)

4. Give dates of treatments .....

5. I certify that he (she) was under my care, TOTALLY disabled and prevented from performing all the duties of his (her) occupation from ..... 19 ..... to ..... 19 .....

6. I estimate further duration of total disability ..... days. (Answer if patient is still disabled).

PREGNANCY

7. If disability due to pregnancy, give probable date of confinement .....

X-RAY

8. Give date X-ray taken ..... What did it disclose? ..... (Please Print)

SURGERY

9. Nature of Operation .....

10. Operation by Dr. ..... When .....

REMARKS

11. .....

Date ..... Signature ..... M.D.

Telephone Number ..... Address .....

is appointed to serve for a period of three months, at the expiration of which time a new group is appointed, and this procedure continues until all members of the society have had an opportunity to serve. Fees for these examinations are paid directly by the insurance company to the examining physician. All specialists are in a separate group, and are asked to examine only those patients whose illnesses fall within their particular fields.

When a patient has lost time in excess of the reasonable disability for his illness, the attending physician is called either by a representative of the plant medical department or the insurance carrier to determine whether or not an impartial examination is indicated. If it is agreed that such examination should be made, an appointment is arranged for the patient at the office of one member of the current panel who is provided in advance of the examination with a form containing the name, diagnosis, duration of disability to date, and name of the attending physician. The examination form is extremely simple, and in most instances may be completed in a very few minutes. The examiner may obtain additional information from the attending physician at his own discretion, and the information provided on the form determines whether or not payments are to be continued or terminated. Failure of the patient to appear for the examination without a reasonable excuse results in suspension of payments.

This plan has been well received and appears to have merit for several reasons:

1. In those cases in which benefits are obviously being abused, it relieves the family physician of the odious task of refusing to certify unwarranted disability.

2. Since the examination is made by a representative of the medical society who is serving for a period of a few months only, it is "impartial" in the eyes of the patient. This is the sole reason for the use of the term, since it is all too often difficult for a patient (faced with the probability of a report not to his liking) to believe that an examination made by a plant physician or a regular examiner for an insurance company is actually impartial. This very fact also eases the position of the examiner who may make it clear that he is in the regular employ of neither.

3. It has met with no opposition from organized labor, which has struggled for years to obtain or increase the benefits of disability insurance for its many members, and therefore has a real interest in the prevention of its abuse by a few.

4. It has been noteworthy that as time passes, word-of-mouth communication being what it is, fewer and fewer of these examinations become necessary. It might even ensue that, providentially and paradoxically, control by this type of examination would by its very existence eliminate its own need for existence.

This method of control, as mentioned above, has proved its

DISABILITY INSURANCE

REPORT OF IMPARTIAL MEDICAL EXAMINATION

Claim Number

Employee ..... Address

Attending Physician .....

Diagnosis

Blood Pressure ..... Pulse ..... Weight

Urinalysis: Reaction ..... Sp. Gravity ..... Albumin

Sugar ..... (if done)

Is patient confined to House? ..... To Bed?

Frequency of Present Treatment

Progress to date .....

Prognosis .....

When in your opinion should claimant be able to return to work?

Remarks .....

Examined this ..... day of ..... 19 .... at My Office / His Her Home

Signed ..... , M. D

Address .....

efficiency in two plants of comparable size (5,000-8,000 employees) in two cities of comparable population (125,000-150,000). In its first full year of operation in the second city the savings in insurance premiums were in excess of $65,000; and this has been the experience in each of the five succeeding years to date.

This plan is not offered as a cure-all for the problems posed by the abuse of group accident and health programs. It is no substitute for basic in-plant preventive medicine and health counselling in the prevention of illness absenteeism. It must be augmented by close claims supervision and an attempt to acquaint the employee who has been guilty of abuse with the total cost of his absence. All of these procedures should work together for good.

Summary

The abuse of group disability insurance is placing an unnecessary and excessive burden on employee benefit plans. The present study, made at two industrial plants whose respective populations were 5,000 and 8,000, suggests that the problem resides principally among female employees between the ages of 20 and 50 years who have excessive sick absenteeism during the summer season. Two measures were devised that resulted in an impressive reduction in the size of the problem. The first of these was a separation of the Employee's Claim Form from the Physicians Report, the latter thus being removed from the claimant's scrutiny. The second was the institution of impartial examinations in questionable cases. Such examinations were performed by a committee whose membership rotated among members of the local medical society.

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THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES

SCHOOL OF NURSING

announces

A PROGRAM OF PROFESSIONAL EVENING COURSES

Most classes will meet one evening a week from 7 to 9:30. Courses scheduled are as follows:

Development and Principles of Industrial Nursing—starting September 10 at the Los Angeles City Health Building. This University Extension course will include an analysis of the nurse's role in industrial in-plant health services.

Management Practices in Hospital Administration—starting September 22 at the Extension Center. Special emphasis will be placed on the exceptional management problems found only in hospitals, and an analysis of personnel relationships.

Industrial Health—starting September 22 at the Extension Center. Discussions of occupational diseases and hazards and plant medical services will be featured.

Public Health Statistics, Counseling and Placement of Hospital Nursing Personnel, and *Vision Screening in the Classroom*—three separate courses, starting September 23 and 24 at UCLA.

A special two-week *Rehabilitation Nursing Workshop* will meet October 19 to 30 at the Rancho Los Amigos Hospital in Downey. Through lectures, conferences, and observations, the workshop is designed to clarify the nurse's role as a member of the rehabilitation team, and to familiarize her more closely with the functions of other members.

Information and applications for all courses and workshops may be obtained through Medical Extension, UCLA Medical Center, Los Angeles 24.

Topical Review

The Toxicology of Some Aliphatic Aldehydes

Edward V. Henson, M.D., South Charleston, West Virginia

THIS third in a series of reviews on the several homologous series of aliphatic chemicals deals with the aldehydes. In the stepwise reduction of acids, which were discussed previously, to alcohols, aldehydes are intermediates.

Most people are not aware of the innumerable contacts they may have with aldehydes in their daily lives. Since this group in the unreacted state has very few household uses, they may be considered rare compounds. Except when one is purchased for some unusual use or for basement experimentation by an amateur chemist, they usually are not identified as such on the labels of containers found in the average storage closet. Since acetaldehyde and glycoaldehyde are normal metabolic products, internal contact with them seems inevitable. Glycoaldehyde[1] tagged with radioactive carbon C^{14} has been shown to be oxidized in the rat to carbon dioxide and can be converted to glycine readily and to formic acid, oxalic acid, and glycogen slowly. Formaldehyde is a commonly used disinfecting and fumigating agent and is the active ingredient in many home deodorizers; so external contact to it is frequent. Air pollution and smog studies have identified many organic compounds, including aldehydes, in contaminated air. Sim and Pattle[2] observed the effect of aldehydes on human subjects and determined their order of conjunctival and nasal irritation. Acrolein[3] is said to be the primary irritant in the exhaust gases from internal combustion engines. It also is a thermal decomposition product of glycerin from fat and probably is an important cause of the irritant effect noted following exposure to the vapors derived from cooking fatty foods over intense heat. Rancid fat also contains a mixture of saturated aldehydes with hexanal, C_6, being the most common.[4] Acrolein and crotonaldehyde are among the volatile substances from freshly crushed garlic and onions.[5] So, although this homologous series is found in gross quantity only in industry, almost everyone appears to have contact with one or more of its members daily.

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Summary of Action

The aldehydes as a group are relatively irritating and toxic substances. In contrast to some other chemical families, the toxicity of the lower members, as measured by the reported LD_{50}, decreases with an increase in the length of the chain. The unsaturated members of the series (5 and 6 of Table I) are much more toxic than the saturated ones (1, 2, 3 and 4 of Table I) with a comparable number of carbons, and they also decrease in toxicity with an increase of molecular weight. The single-dose oral toxicity in grams per kilogram of body weight for rats listed in Table I generally follows this trend.[6] By subcutaneous injection of the aldehydes into mice, Skog[7] obtained the following LD_{50} doses in grams per kilogram of body weight.

Table I—Relation of Aldehydes to LD_{50}

Chemical	Injection LD_{50}	Oral LD_{50}
1. Formaldehyde	0.30	0.8
2. Acetaldehyde	0.56	1.93
3. Propionaldehyde	0.68	1.41
4. Butyraldehyde	6.17	5.89
5. Acrolein	0.03	0.046
6. Crotonaldehyde	0.16	0.22

Skog[7, 8] also studied the anesthetic-narcotic action of the aldehydes by inhalation and subcutaneous injection and observed that the anesthetic activity with unconsciousness decreased with an increase in carbon number. Deaths resulting from the administration of acetaldehyde, propionaldehyde, and butyraldehyde occurred during anesthesia and seemed to be caused by central depression of the res-

piratory center. Although they were somewhat anesthetic, formaldehyde, acrolein, and crotonaldehyde caused marked pulmonary irritation by inhalation, and deaths were often delayed until the effects of lung injury developed. By subcutaneous injection there seemed to be an inverse relationship of the length of the chain to the rapidity of onset and duration of anesthesia. When death occurred, the survival time was longer following the injection of the longer-chained members.

Hematuria and nephrotic changes in the kidneys were observed after the injection of butyraldehyde. Injection of crotonaldehyde caused an intense stage of excitement and reddening of peripheral parts of the body.

Skog observed an elevation in blood pressure by all the aldehydes which he studied except formaldehyde. Wingard et al.[9] reported that intravenous injection of the simple aliphatic aldehydes caused a pressor response similar to that of epinephrine in dogs under barbiturate anesthesia. The branched compounds, the higher aliphatic aldehydes, the substituted aldehydes, and the ring compounds were depressors, sometimes with a pressor phase. Romano et al.[10] stated that the straight-chain aldehydes, including hexanaldehyde, were all pressor substances. Isobutyraldehyde was two-thirds as active as butyraldehyde. A propionaldehyde-arterenol compound was demonstrated in vitro by chromatography, and the authors suggested that aldehydes act by forming a base with arterenol, the effects depending upon the stability of the base.

Larson, Finnegan, and Haag[11] studied the edema-producing potencies (EPP) of chemicals in water solution by instilling the solutions into the upper conjunctival sac of the eyes of rabbits. With the exception of formaldehyde, among the saturated aldehydes increasing molecular weight resulted in increasing EPP. Unsaturation markedly increased the EPP of aldehydes; but in contrast to the saturated compounds, four-carbon crotonaldehyde was less active than three-carbon acrolein.

Sim and Pattle[2] observed that 0.8 ppm for 10 minutes and 1.2 ppm for 5 minutes exposures to acrolein caused severe mucous membrane irritation in human subjects. Both exposures were barely tolerated for those times. Lacrimation appeared in 20 and 5 seconds respectively. Crotonaldehyde at 4.1 ppm for 15 minutes was highly irritating, with lacrimation appearing in 30 seconds. Formaldehyde at 13.8 ppm and acetaldehyde at 134 ppm for 30 minutes were less irritating. Propionaldehyde, butyraldehyde and isobutyraldehyde at 134, 230, and 207 ppm for 30, 10, and 30 minutes respectively were not irritating. The decreasing order of irritation as shown in this study was: acrolein, crotonaldehyde, formaldehyde and acetaldehyde. The higher molecular weight compounds were not irritating at the concentrations studied.

The aldehydes are capable of producing both local cutaneous sensitization and general systemic allergic reactions. Of the aldehydes, formaldehyde is most commonly incriminated as a causative agent of contact dermatitis. It is difficult to determine whether this is solely a reflection of the fact that its more extensive use affords greater opportunities for contact, that it may be the most conspicuous contaminant in the environment, or that it reacts more readily with proteins to form allergens. Mumford and Auckland[12] reported an interesting case of an English woman who repeatedly developed acute dermatitis of her face and neck following exposure to burnt coal-gas. They were able to demonstrate that incompletely combusted coal-gas caused the dermatitis. A 0.5% solution of formaldehyde in water gave a positive patch test reaction, and the authors thought that the aldehydes formed by the incomplete combustion of the gas were the cause of the dermatitis. Rappaport and Hoffman[13] reported a case of a young man who had demonstrable sensitivity to many aldehydes. He first developed urticaria on the terminal phalanges of the second and third fingers of his right hand and swelling of his lips. In about a week the hives became generalized. After an extensive study during the 15 months that the symptoms persisted, reexamination of the history led the authors to consider cigarette smoke as the cause of the urticaria. They were able to show that smoking cigarettes which contained glycerin as a hygroscopic agent caused hives while cigarettes containing diethylene glycol did not. Entering a smoke-filled room or shaking hands with someone who had been smoking could produce symptoms in a few minutes. Eating food cooked by broiling produced generalized urticaria, while the same food prepared in some other manner did not cause urticaria. A drop of a 1:1,000,000 solution of formaldehyde placed on the lip produced local urticaria in a few minutes and mild generalized urticaria in 10 minutes. Intramuscular injection of 0.02 cc. of a 1:10,000,000 solution produced urticaria in 35 minutes. When formaldehyde was given orally in gelatin capsules, slight symptoms occurred with 1 drop of a 1:1,000 solution and definite urticaria with the 1:100 solution. Other aliphatic aldehydes were tested by applying a few drops to the lip with a glass applicator. All the saturated aldehydes up to stearic alde-

hyde (C_{18}) produced an urticarial reaction. As the number of carbon atoms increased, the concentration required to produce a reaction was proportionately greater. The range of dilution varied from 1:1,000,000 for formaldehyde to 1:1 for the 18-carbon aldehyde. Aromatic aldehydes and conjugated aliphatic aldehydes, except acrolein, gave negative results. A conjugated chemical is one which has alternate double bonds in the structure, as acrolein (C=C—CHO) and crotonaldehyde (C—C=C—CHO). The authors theorized that the saturated aldehydes joined with body protein to produce the allergen to which the patient was sensitive and aromatic aldehydes and conjugated aldehydes did not appear to be able to make allergens with protein.

The Chemistry of the Aldehydes

The homologous series of saturated aldehydes has the general formula $C_nH_{2n}O$ and is characterized by the presence of a carbonyl group (C=O), a grouping which is also the functional unit of ketones. An aldehyde, $RC\overset{=O}{\underset{-H}{}}$ has one hydrogen and one alkyl radical attached to the carbonyl carbon while a ketone, R_2CO, has two alkyl radicals attached to the carbonyl group. The carbonyl group is able to add a great many reagents, and its reactivity is altered by the attached radicals. Aldehydes which have a hydrogen on the carbonyl are much more reactive than ketones with their two alkyl groups. Formaldehyde, HCHO, has two hydrogens on the carbonyl grouping; so perhaps some of its unusual characteristics are due to this structural feature.

The name aldehyde, unless modified by a prefix, means acetaldehyde, which is formed by the oxidation, or dehydrogenation, of alcohol. The word aldehyde is said to be a contraction of *al*cohol *dehyd*rogenated. The common names of the aldehydes are taken from the acids to which they are converted by oxidation. The aldehydes are thus intermediate products in the oxidation of alcohols to acids. The common names are usually used to identify the simpler aldehydes, while the Geneva system is used to name the more complex molecules. The Geneva system of nomenclature adds -al to the parent hydrocarbon of the respective aldehydes. An -enal indicates an aldehyde derived from an ethylenic hydrocarbon and -ynal one from an acetylenic hydrocarbon. The straightchain aldehydes, like the fatty acids, have the functional group at the end of the molecule. When both terminal carbons are carbonyl groups, they are dialdehydes. A whole series of dialdehydes are known. The first three members are shown in the table below. Table II illustrates the relationship of the two nomenclature systems.

Table II—Relation of Structure to Nomenclature

Formula	Common Name	Geneva Name
HCHO	Formaldehyde	Methanal
C—CHO	Acetaldehyde	Ethanal
C—C—CHO	Propionaldehyde	Propanal
C=C—CHO	Acrolein	Propenal
C≡C CHO	Propargylic aldehyde	Propynal
C—C—C—CHO	Butyraldehyde	Butanal
C—C=C CHO	Crotonaldehyde	Buten-2-al
OHC—CHO	Glyoxal	Ethandial
OHC—C—CHO	Malonic aldehyde	Propandial
OHC—C—C—CHO	Succindialdehyde	Butandial

Although aldehydes ordinarily do not form stable hydrates, in water solution they probably exist in equilibrium with their hydrates. An exception is chloral, trichloracetaldehyde or trichlorethanal, which forms a stable crystalline material, chloral hydrate, a common hypnotic. The fact that this compound does not react as do other aldehydes is evidence that a molecule of water has been added to the carbonyl group, thus modifying its action.

Since many of the aldehydes are highly reactive compounds, the molecules tend to react with one another to form more stable and less reactive substances. The process by which molecules react with one another to form higher molecular weight substances is called polymerization. Three units of formaldehyde react to form a cyclic compound called trioxane. Paraform, or paraform aldehyde, a white solid, contains more than 100 formaldehyde units. Polymerization of acetaldehyde yields paraldehyde, a trimer, and metaldehyde, a tetramer. The higher molecular weight aldehydes are less reactive and have less tendency to polymerize.

The boiling points of the aldehydes increase with increasing molecular weight, and for the unbranched, saturated members the increment of increase is approximately 25°C. for each additional carbon in the chain. They vary in form from gaseous formaldehyde to solids at C_{12}. The lower members of the series are soluble in water and above C_5 are insoluble or only slightly soluble in water. The short aldehydes have a sharp penetrating odor, the medium-length members are more ethereal, and the solids are odorless.

In the following paragraphs some representative aldehydes are discussed in detail.

Formaldehyde

Formaldehyde, methanal, HCHO, is a color-

The chemical information used throughout this article was obtained from Fieser and Fieser[14] and Whitmore.[15]

less gas with a characteristic, irritating odor. Because of its extreme reactivity and ability to combine with practically all other classes of chemicals, formaldehyde has great industrial importance. As a 35 to 40% solution in water and methanol it is known as "formalin," which is used in embalming fluid, as a preservative for anatomical specimens, and as a hardening agent of photographic film. This aldehyde has extensive industrial use in the manufacture of phenol-formaldehyde, urea-formaldehyde, thiourea-formaldehyde and melamine-formaldehyde resins. Disinfection by formaldehyde fumigation has limited application and cannot be relied upon to achieve sterilization. Small-scale fumigation is often carried out by burning paraform candles, which depolymerize to formaldehyde. With ammonia this aldehyde condenses to form a crystalline solid known as hexamethylenetetramine, methenamine, hexamine, or urotropin which is used as a urinary antiseptic. In acid urine the condensation reaction reverses, and formaldehyde is released slowly.

In 1945 the U.S. Public Health Service[16] published a pamphlet on formaldehyde which summarized its toxicology and physiological effects. Formaldehyde is absorbed rapidly by all routes of administration and can be found for only a short period at the site of administration. Following inhalation, it disappears rapidly from the blood. It has a great affinity for proteins, to which it is readily bound. It is gradually oxidized to formic acid and is partly excreted as formate in the urine. The formic acid may also be oxidized slowly to carbon dioxide and water.

Exposure to formaldehyde vapors causes irritation of the mucous membranes of the eyes and respiratory tract. The total effect is naturally determined by the time-dose factor. Instillation of aqueous solutions into the eyes of experimental animals causes lacrimation, conjunctivitis, keratitis, ulceration, and iritis. Ingestion of formaldehyde causes initial respiratory stimulation, followed by depression. Small doses may have a direct stimulating effect on the heart, while larger doses cause a fall in blood pressure, probably by interfering with the cardiac nerve supply. There is some question whether the observed hemolysis of red blood cells is caused by formaldehyde or by formic acid which is present as a contaminant or formed in the body. Small oral doses may cause a slight increase in kidney function, and intestinal tract symptoms may be absent. Daily doses up to 200 mg have been given with only slight irritation of the upper intestinal tract. Larger amounts cause severe inflammation of the stomach, duodenum, and jejunum associated with abdominal pain, cramps, nausea, and vomiting. Ingestion of a fatal dose is followed by intestinal symptoms, dyspnea, unconsciousness, and failure of circulation. If death is delayed, uremia may develop from damage to the kidneys.

Fatalities have resulted only from the ingestion of aqueous solutions of formaldehyde by mistake or with suicidal intent.

Many industrial cases of irritation of the eyes, respiratory tract, and skin have been reported. One author lists the frequency of symptoms as bronchitis, dermatitis, rhinitis, oropharyngitis, and conjunctivitis.[16] The threshold limit for an eight-hour day is 5 ppm.[26]

Acetaldehyde

Acetaldehyde, ethanal, CH_3CHO, is a highly reactive, volatile (b.p., 21°C), colorless, mobile liquid with a pungent ethereal odor. It is readily soluble in water, alcohol, ether, and many aliphatic and aromatic hydrocarbons. It is easily oxidized to acetic acid, reduced to ethyl alcohol, and combines with amines to form dyestuffs, rubber accelerators, and antioxidants. Resins made by the condensation of acetaldehyde with phenol and urea are more pliable than those made with formaldehyde and have particular application in enamels and varnishes. Industrially, this aldehyde has great use as an intermediate in the manufacture of many higher molecular weight aldehydes, alcohols, and acids. The threshold limit is 200 ppm.[26]

Pharmacologically, acetaldehyde is an anesthetic and sympathetic stimulant. Koppanyi[17] studied its anesthetic effect on dogs by using the vapors from a 30% solution in water. The animals were completely relaxed in five minutes, and anesthesia was maintained easily for one hour or more. Recoveries were fairly rapid—the animals would stand unsupported within one hour and showed no ill effects. During inhalation there was an increase in the rate and depth of respiration and a fairly rapid and significant rise of blood pressure. The author concluded that for animal experimentation acetaldehyde may be a useful, rapidly acting narcotic and that it is a sympathetic stimulant that produces all the findings of typical thoracolumbar excitation. Derbes and Martin[18] observed the effects of acetaldehyde on perfused lungs and coronary vessels of animals. Bronchioles constricted by histamine were relaxed, as were bronchioles constricted by antigen in perfused lungs from sensitized guinea pigs. Coronary vessels constricted by alphahypophamine (Pitocin) were also relaxed by the aldehyde. These effects are the same as those

obtained by using epinephrine; however, 5 cc of a 5% solution of acetaldehyde did not exert as powerful an effect as 0.2 cc of 1:10,000 epinephrine solution. A striking therapeutic effect[19] upon the circulation by this aldehyde has been reported following its oral and parenteral use in moribund patients.

In the animal body ethyl alcohol seems to be oxidized to acetaldehyde, but the metabolic fate of the aldehyde is uncertain. Lublin and Westerfeld[20] studied its metabolism in cats after different organs had been removed and observed that the liver was the primary site of its metabolism, and the acetoin (acetyl-methyl-carbinol) pathway played a minor role in its metabolism.

In the past few years chemical metabolic blocking agents have been used in the treatment of chronic alcoholism. It is thought that the metabolism of alcohol is blocked at the acetaldehyde stage, and the accumulation of the aldehyde produces the unpleasant symptoms which deter the patient from consuming alcoholic beverages. Asmussen[21] determined that normal blood contains less than 0.04 mg % of acetaldehyde. Intravenous injection of acetaldehyde to produce concentrations of 0.2 to 0.7 mg % caused symptoms identical to those which occurred in subjects who drank alcohol after being pretreated with tetraethylthiuram disulfide, one of the blocking agents. The symptoms included flushing of the face, increased skin temperature, headache, and palpitation of the heart.

Paraldehyde

Paraldehyde is a polymer containing three molecules of acetaldehyde arranged heterocyclically so that the functional activity of the aldehyde radical is absent. When heated in the presence of a trace of mineral acid, it depolymerizes to acetaldehyde. Thus it serves as a convenient source of acetaldehyde without being concerned with the problems of acetaldehyde volatility and flammability. It is a colorless, clear liquid with a characteristic odor and a disagreeable taste. Although it is a very effective hypnotic which can be administered orally, rectally, or intramuscularly, its odor and taste prevents general patient acceptance. The usual dose of 3-8 cc produces normal sleep in 10-15 minutes. Although paraldehyde is considered a safe drug—120 cc was given rectally without a fatality—as little as 31 cc rectally has caused death.[22] Since it seems to be metabolized in the liver, impairment of liver function may account for the death. The metabolic pathway is thought to be as follows: paraldehyde, acetaldehyde, acetic acid, carbon dioxide, and water.[23]

Acrolein

Acrolein, acrylaldehyde, acrylic aldehyde, propenal, C=CCHO, is a colorless liquid which boils at 52.4°C and has a pungent, offensive odor. Because of its sharp penetrating odor it has been used in methyl chloride refrigerating systems as a warning agent. Both the double bond and carbonyl group are reactive, and their conjugation increases the reactivity of both. It is a raw material in the manufacture of pharmaceuticals, perfumes, food supplements, and resins.

Henderson and Haggard[24] reported that 1 ppm was detectable immediately, 5.5 ppm caused irritation, and 10 ppm may be lethal in a short time. These opinions are confirmed by the observations of Sim and Pattle[2] mentioned previously. That acrolein is a very toxic material is reflected in the recommended threshold limit of 0.5 ppm. However, because it causes intense irritation of the conjunctiva and upper respiratory tract, warning is adequate to prevent serious exposure.

Crotonaldehyde

Crotonaldehyde, crotonic aldehyde, buten-2-al, C—C=C—CHO, is a colorless liquid with a sharp, irritating odor. It has a molecular weight of 70.09 and boils at 102.3°C. It is an intermediate in the commercial production of butyraldehyde and butyl alcohol and condenses with amines to form antioxidants and accelerators. Because of its odor and effect on mucous membranes, it has been used as a warning agent in gas systems. These same properties also warn workers and prevent excess exposures. Crotonaldehyde can be made easily from acetaldol, C—COH—C—CHO. It was the use of acetaldol on lettuce and its conversion to crotonaldehyde which caused severe irritation among lettuce handlers.[25] The single oral LD_{50} dose for rats in grams per kilogram has been determined as 0.22. Although this aldehyde has some bactericidal activity, its practical effectiveness seems to be low.[5]

Glyoxal

Glyoxal, ethanedial, oxaldehyde, biformyl, OHC—CHO, is the simplest dialdehyde. It is a yellow liquid which tends to polymerize spontaneously. Since it has two functional groups, its primary industrial use is to cross-link proteins and starch in such applications as sizing paper, making washable wall paper, and treating the glue surface of envelopes. When applied to fabrics, it increases their resistance to creasing and shrinking. It has been used as a substitute for formaldehyde in embalming fluids.

Glyoxal vapors do not irritate the skin or mucous membranes, and the liquid does not burn the skin, although it may discolor it. There appears to be very little hazard from using glyoxal, and reports of ill effects have not been noted.

Comment

In this review the actions of the aldehydes in relation to one another and the actions of representative members have been summarized. Local irritation by all the aldehydes seems to prevent dangerous exposures, particularly to the more toxic unsaturated compounds, and the absence of clinical reports would indicate that chronic intoxication does not occur.

Dr. Henson's address is Union Carbide Chemicals Company, South Charleston 3, W. Va.

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EIGHTY-SEVENTH ANNUAL MEETING

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AMERICAN PUBLIC HEALTH ASSOCIATION

will be held

October 19-23, 1959

Atlantic City, New Jersey

International Symposium on Maximum Allowable Concentrations of Toxic Substances in Industry

Presented by the Permanent Committee and International Association on Occupational Health, International Union of Pure and Applied Chemistry

PRAGUE—APRIL 14-17, 1959

Reported by

William B. Deichmann, Ph.D., F.R.S., and Horace W. Gerarde, Ph.D., M.D.

Because of the general interest in learning what was reported at the International Symposium, the section of this Journal usually reserved for abstracts of current literature is devoted to abstracts and summaries of the papers presented at this important meeting.—Editor

Methods Used by the Committee Z37 of the American Standards Association in Establishing Maximal Acceptable Concentrations of Toxic Dusts and Gases. W. F. von Oettingen. Public Health Service, National Institutes of Health, Bethesda, Md.

The author reviewed the establishment and functions of Committee Z37 of the American Standards Association in 1938 under the chairmanship of W. P. Yant. He discussed the meanings of the terms "maximum allowable" and "maximum acceptable" concentrations and finally pointed out that "standards refer to what is considered a moderate climate and persons having a fairly normal diet, but it is conceivable that under extreme climatic conditions such as excessive cold or heat and with deficient nourishment or excessive intake of fats or other nutrients, alcoholic beverages and drugs, the physiological functions of the human organism and its susceptibility to certain toxic substances may vary considerably, so that such maximal acceptable concentrations may not hold true for all climates or nations."

The Relationship of Atmospheric MAC's to Permissible Concentrations in Urine. H. B. Elkins. Division of Occupational Hygiene, Massachusetts Department of Labor and Industries, Boston.

There are fundamentally two methods of establishing permissible concentrations of toxic substances in urine. The first is the direct one of correlation of urinary concentration with symptoms or other indications of intoxication. The second consists of relating urinary concentrations to atmospheric concentrations.

The first consideration in establishing urinary MAC's is the proper unit of measurement of concentration to be employed. Uncorrected concentrations (weight per unit volume) are unreliable because they are so greatly affected by water balance. Concentrations based on time of secretion are difficult to obtain, and their validity is questionable unless corrections are made for the size and, possibly, the rate of activity of the subject. The two components to which the concentration of toxic substances has been most successfully related are total solids (specific gravity) and creatinine content.

In using urinalysis data to evaluate exposures, it is important to know the significance of the efficiency of the body as a sampling device. It is well known that if a number of workers in a given environment are tested by urinalyses, the variation in the results will be much greater than the apparent variation in the exposure. This may be due in part to greater absorption by some workers. To this extent the urinalysis is a more accurate means of evaluating hazard than is air analysis. A number of the variations, however, are due not

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to the differences in absorption but to differences of the proportion of absorbed material which is excreted. When two workers absorb the same amount of toxic agent but excrete different amounts, it is not known which one is in the greater danger of intoxication.

It is much more convenient to collect small samples than to obtain 24-hour specimens, and while, in the majority of cases, the rate of excretion is fairly consistent, there are exceptions which to date have not been explained. At present a study is being made of this problem in an effort to improve the reliability of urinalysis of spot samples as a method of evaluation.

Problem of Testing for Dietary Carcinogenicity. W. B. Deichmann. Department of Pharmacology, University of Miami School of Medicine, Coral Gables, Fla.

For the precarcinogenic testing of food additives, it is suggested that studies be initiated as follows:

1. Feed each compound to as many species (mammals) and for as long a period of time as possible, including at least the rat and the dog and preferably other animals—not necessarily those used widely in the past.
2. Start feeding the compound to weanling males and females.
3. Feed pregnant females and conduct reproduction studies.
4. Start groups large enough to provide a significant number of survivors living to a ripe old age.
5. Give careful consideration to the feeding of a well-balanced basic diet, one that will neither inhibit nor support the formation of cancer.
6. Consider administering the compound at the same time by several other routes (application to the skin, subcutaneous injection, etc.).
7. Maintain an adequate control group.
8. Add to these fundamental requirements some consideration of the strains to be used. Evaluation of the data will not always be an easy matter, since spontaneous tumors will appear, at different sites, in treated and in untreated animals. Hence, an adequate number of control animals is critically important. If the results are significantly positive in a rat, dog, pig, monkey, etc. feeding experiment, then there is no question that the compound must be condemned as a food additive. If the results of the feeding experiment are inconclusive, then the data of cutaneous, subcutaneous, or other studies may well provide the answer. If only one mode of administration other than ingestion should induce a significant number of malignant tumors, then the data need careful evaluation. Whether such information should or should not eliminate a compound as a food additive will have to depend on the species used, doses administered, method of administration or implantation, and other factors such as the importance of the contemplated use of the additive—whether it is to be added to maraschino cherries, chewing gum or dill pickles, or to foods such as milk and meat.

United States' Experience with Proposed Safe Levels of Exposure to Toxic Beryllium Compounds. Harriet L. Hardy. Occupational Medical Clinic, Massachusetts General Hospital, Boston.

In the United States there are in current use three separate figures to control harmful effects of toxic beryllium compounds, and so far as is known, this is unique in industrial hygiene practice.

The target level intended to prevent acute beryllium poisoning is 25 $\mu g/M^3$ of air for a short exposure. No time is given, and physicians are not altogether satisfied with this aspect of the figure. There seems to be fairly universal agreement among United States industrial hygienists that 25 μg Be/M^3 of air is a safe level.

The figure used as the maximum allowable concentration for a 40-hour a week exposure is 2 $\mu g/M^3$ of air for an 8-hour day average. By stating the maximum allowable concentration in this fashion, it will be seen that the 25 $\mu g/M^3$ for short exposure is made more realistic. Neither limit shall be exceeded for the conditions stated. In current practice in the United States those responsible for the control of exposure to toxic beryllium compounds, where possible, hold all exposures at or below the level of 2 $\mu g/M^3$ of air, regardless of the duration of the operation.

Eisenbud, of the New York Office of the Atomic Energy Commission, and a number of members of the Beryllium Advisory Committee proposed the figure of 0.01 $\mu g/M^3$ of air for a weighted monthly average as the safe level of exposure to toxic beryllium compounds of people living near a beryllium-using plant. Experience in three states with fifty-odd cases of neighborhood beryllium disease confirms the reality of such a hazard. It is possible that a number of clinically mild cases of beryllium poisoning have escaped detection in studies of communities near beryllium plants. The fact is that there are only 44 well-documented cases of persons who suffered chronic beryllium intoxication without ever going into a beryllium plant. This group has the high mortality rate of 53%. The figure Eisenbud proposed took into consideration a 24-hour daily exposure, if a hazard existed, and exposure to children.

The Investigation of Present Time Definitions and Conceptions of Maximum Allowable Concentrations in Different Countries. W. L. Ball. Investigations Group, Occupational Health Division, Department of National Health and Welfare, Ottawa, Canada.

Impurities in industrial chemicals may increase or decrease their toxicities. Synergism and antagonism must be considered. Toxicity estimation should be based on normal working hours. Short-term exposures to highly toxic substances are dangerous even when they do not increase the

daily average beyond the acceptable limit. Discomfort may be the basis for an MAC when this is experienced below the hazardous level. Stress decreases the body's ability to withstand toxic concentrations of substances. The toxicity of a mixture may be the sum of the toxicities of its ingredients, but synergism and antagonism sometimes occur. Unusually sensitive employees must be protected from contact with certain chemicals.

Safe Levels of Dustiness in Cotton Spinning Mills. R. S. F. Schilling and S. A. Roach. Occupational Health Unit, London School of Hygiene and Tropical Medicine, England.

The prevalence of byssinosis was measured in three coarse- and two fine-cotton mills and compared with the dust concentrations to which the workers were exposed. Prevalence was related closely to the over-all dustiness but not to the concentrations of fine dust (less than 7 μ). The prevalence was lower in the older workers than in the younger workers for similar dust exposures, presumably because the older workers tended to leave the mills because of the ill effects of the dust.

It appears that a mill with a concentration of 100 mg./100 M^3 or less could be regarded as comparatively safe from the risk of byssinosis. (Revised from the author's summary)

The Metabolism of (C^{14})-Ethylene Glycol. P. K. Gessner and R. T. Williams. Department of Biochemistry, St. Mary's Hospital Medical School, London.

In rats, oxalate (0.25% to 1% of the dose) was found in the urine when the dose of glycol was 1 gm/kg or more. When the dose was 0.1 gm/kg, oxalate excretion was negligible. Rats excreted more of the dose of C^{14} in the urine than did rabbits, and the amount of radioactivity in the urine varied with the dose, being 21% at 0.1 gm/kg and 78% at 7.5 gm/kg.

In guinea pigs, no oxalate was found in the urine with doses of 1.3 and 2.7 gm/kg of the glycol, but a cat receiving 1 gm/kg excreted 0.9% of the dose as oxalate in 48 hours. Our results suggest species differences in the amount of oxalate produced, rats and cats forming oxalate from the glycol more readily than rabbits and guinea pigs.

The distribution of radioactivity in the tissues of rats 24 hours after dosing with the glycol showed that the concentration of C^{14} was highest in the bones (2% to 10% of the dose). This suggests oxalate formation and deposition in the bones. In the rabbit, the highest radioactivity was found in muscle, liver, and bone, but bone (1.7%) was not significantly higher than liver (1.4%) and muscle (3.4%).

These experiments suggest that the main path of metabolism of ethylene glycol leads to carbon dioxide via glycolaldehyde, glycollic acid or glyoxylic acid. There is a minor path which leads to oxalate. The significance of the minor path, which leads to a toxic metabolite, depends upon dose and species of animal.

Abstracts

Experimental Methods Used as a Basis for Determining Maximum Allowable Concentration. J. M. Barnes. Toxicology Research Unit, M. R. C. Laboratories, Carshalton, Surrey, England.

Animal tests will continue to provide a basis for assessing the potential toxicity of a substance to which man is liable to be exposed. As many different species as possible should be exposed to the acute effects of the material. If wide species differences in sensitivity are found, the extrapolation to man must be correspondingly more cautious. If considerable species difference in sensitivity do exist, this suggests that the compound being administered must first be metabolized and it is some metabolite that is responsible for its toxic action.

The short-term experiments must be used to determine the main site of action of the toxic substance. In the case of the material we are considering there are three: (*a*) a direct irritant and destructive action on the tissues of the respiratory passages and the lungs; (*b*) a narcotic action, presumably on the central nervous system, and (*c*) a toxic action on the liver and/or kidneys.

Repeated exposures must be given in order to study cumulative effects. There seems no good reason for prolonging such tests for more than two to three months unless changes such as weight loss and deaths are first seen only at that time.

Mortality, growth rate or body weight change, and relation to liver and kidney, are essential first criteria of poisoning. Improvements might be made along the following lines, depending on the nature of the most important site of action.

In the lungs, more attention should be paid to the earliest lung and respiratory tract lesions. Function studies, such as gas transfer, might be considered. Reference was made earlier to the possible role of respiratory tract irritants in awaking or enhancing the effects of pathogenic bacteria. Controlled infections must be used for the study of any such effects. This is a new field and its value or importance cannot be assessed.

For those substances acting on the central nervous system, pathology and biochemistry seem to have little to offer as means of detecting minimal effects. Tests of function—behavior studies, etc. —appear likely to offer most help.

For those materials damaging the liver and kidneys, organ weight changes, though apparently crude, have been shown to be as sensitive a method as can be suggested for detecting change.

The Investigation of Vapor Toxicity. J. C. Gage. Imperial Chemical Industries Ltd., Industrial Hygiene Research Laboratories, The Frythe, Welwyn, Herts.

In the routine laboratory investigation of the vapor toxicity of volatile liquids, it is necessary first to ascertain whether a nearly saturated vapor produces any toxic effects on experimental

animals. Particular attention should be directed to subacute effects arising from repeated daily exposures for a period of at least three weeks. If any toxic action is thereby revealed, groups of animals are exposed to a series of diminishing concentrations. This will enable one to ascertain the level at which no effect is produced after repeated exposures for at least three weeks.

Exposure chambers have been developed in which experimental animals can be exposed to known concentrations of toxic substances. A dynamic method of preparing the test atmospheric concentrations is much to be preferred to a static one. A convenient method of continuously generating a vapor concentration of a volatile liquid involves injecting the liquid at a known rate into a metered stream of air by means of a controlled fluid-feed atomizer. This method may be modified to permit the preparation of low dilutions of gases. Mists and dusts may be prepared if the atomizer is used to inject solutions of nonvolatile liquids and solids in inert volatile solvents. A different approach is necessary for preparing dispersions of insoluble dusts.

The exposure chambers described have been modified and permit continuous exposure of small animals with continuous collection of excreta for metabolism studies.

Analytical Methods for Measuring the Concentration of Toxic Substances in Industrial Atmospheres. J. C. Gage.

An examination of the industrial hygiene literature shows a tendency toward a regular decrease in the values of the maximal allowable concentrations. There is no evidence to attribute this to an increase in sensitivity of the working population. It is due to a greater preoccupation with the subtler effects of prolonged exposure and to the greater probability that hypersensitive individuals will be encountered with the more prolonged use of a chemical. In spite of this tendency, the purely analytical considerations make it desirable that a maximal allowable concentration should always have a finite magnitude and never be placed at zero. Nevertheless, when the toxicological evidence is particularly incomplete or uncertain—and this applies particularly in the case of known or suspected carcinogens—it would be appropriate to annotate the figures with the comment that they are liable to be drastically reduced if new information becomes available.

To sum up, there is an interaction between maximal allowable concentrations and the analytical methods used for industrial hygiene air analysis. A close collaboration between toxicologists and analysts is desirable, and the selection of analytical methods should be undertaken only by those who are conversant with the special problems involved. The Toxicology and Industrial Hygiene Division of the International Union of Pure and Applied Chemistry is composed of such individuals at the international level, and it would welcome the collaboration of other experts.

Factors Modifying the Toxicity of Manganese Minerals. J. Rodier. Section for Protection against Radiation, Atomic Center of Marcoule, France.

The authors discuss the influence of particle size and the manganese content of particulates on the health of workers employed in manganese mining operations. Atmospheres containing 1,000 5-μ particles per cubic meter of air and a manganese content of 50 mg per cubic meter of air are regarded as safe for repeated daily exposure (tolerable limit). These levels do not completely eliminate the danger of manganese intoxication. A table is presented giving the particle sizes and the number of particles per cubic meter of air for two manganese-containing minerals (tiouine and imini).

Variations of CO in a Coking Plant. F. Borbely. Legal Medical Institute of the University of Zurich.

Analytical determinations were carried out over a period of two years. Values of CO varied considerably at different sites of operation. The American MAC value of 100 ppm was often exceeded; frequently more than 10 times. In spite of such high values, concentrations of COHb in blood never exceeded 10%. The mortality rate and causes of death of these industrial workers (exposed for a period of 21 years) were no different from those of other people in the community.

Equipment for the Continuous Determination of Solvents in Air. D. Hogger. Industrial Medical Service, Bundesamt für Industrie, Gewerbe und Arbeit, Zurich.

A sampling device carried by the workman (on his back) during the entire working day, collects air from an area near the face at the rate of 0.5 to 1.0 liter per minute. A second apparatus (stationary) determines and registers the concentration of a solvent in air every two minutes.

The Physiological Effects of Trichlor-Ethylene on the Conditioned Responses in the Rat. E. Grandjean. Institute of Hygiene and Physiology of the Federal Polytechnical School, Zurich, Switzerland.

The effects of trichlorethylene (TCE) on the conditioned response in the rat were studied in order to obtain information on the limiting concentrations necessary to produce early effects on the central nervous system. Rats were exposed 4 to 11 weeks (7 hours per day to concentrations of 200 ppm) and the reaction time recorded after each daily exposure. A prolongation of the average reaction time was observed which was statistically different from the controls for the entire period of exposure to TCE. In two other experiments, the conditioned responses to fear and hunger were measured after exposure to TCE at 200 ppm and 800 ppm.

The author concludes that the simple conditioned responses to fear and to hunger are not sensitive methods for studying the effects of TCE on the

nervous system. These functions are localized in subcortical structures, which are not affected by low concentrations of the solvent.

Correlation Between Exposure Concentrations and Concentrations in Biological Materials. E. Grandjean. Institute of Hygiene and Physiology of the Federal Polytechnical School, Zurich, Switzerland.

Studies were conducted on the relationship between air concentrations and urinary output of trichlorethylene, mercury, and lead in workers exposed to these chemicals.

The author states that urinary trichloracetic acid is not a reliable test for exposure to trichlorethylene. The conclusion is based on studies of 73 workers in 24 different working areas. Approximately 13% of the trichlorethylene inhaled is excreted in the urine as trichloracetic acid.

The determination of mercury in the urine and/or blood was not found to be a reliable test for exposure to mercury in the working environment. The conclusion is based on studies of 54 workers.

The concentration of urinary lead is regarded as a reliable test for exposure to lead in the working atmosphere. The tolerable limits recommended are as follows: air, 0.15 mg/m^3; blood, 0.05 mg/100 gm; urine, 0.15 mg/liter.

A New Polarographic Method for Determinating Manganese Traces in Industrial Atmospheric Suspension. P. Sanz-Pedrero. Institute of Industrial Medicine and Security, Madrid, Spain.

1. Manganese, on a supporting solution of 0.1N Na_2SO_3, is manifested with a cathodic reduction wave at a half-wave potential of E $\frac{1}{2}$ = 1.54 volt in relation to the S.C.E. at 22°C. Using this supporting solution, the oxygen in solution shows no interference since it is quickly eliminated.

2. There is a perfect linear relationship between the concentrations of Mn tested, 0.55/ml, and the diffusion intensities. This polarographic method is proved to be more sensitive and accurate, working at such low concentrations, than the photocolorimetric method by oxidation to permanganate generally used to determine Mn.

3. There is no interference in the polarographic determination of Mn in the presence of Cd, Cu, As, Pb, Ca, Fe, and phosphates, in higher and lower concentrations than those of Mn.

4. The analyses of the sample tested prove the accuracy of the polarographic method when the diffusion intensity increases are used instead of the standard curves for the evaluation, since the errors never exceed 5%.

5. This method can be used with great efficacy for the determination of Mn in dust and fumes on account of its great sensitivity and accuracy, and also because the elements with which it may be in contact in the samples do not interfere.

[AUTHOR'S SUMMARY]

Concepts in Italy Regarding Maximum Allowable Concentrations in Industry. L. Parmeggiani. Clinica del Lavoro "Luigi Devoto," University of Milan, Italy.

The concept of the MAC for toxic substances in industry does not yet appear to be well defined. In Italy, the opinion prevails that the values will protect all workers against possible health effects excluding allergic conditions and purely subjective responses. There is a need for establishing MAC's for acute exposures, having maximum limits which should not be exceeded even for very brief periods. The MAC's should apply only to chemicals in the air which can be absorbed into the blood through inhalation. Chemicals absorbed through the skin should not be included in the MAC list. Limits for these chemicals should be set on maximum concentrations in the urine.

So-Called Maximum Biological Allowable Limits. E. C. Vigliani. Institute of Occupational Health, University of Milan, Italy.

In some instances, the determination of toxic substances in biological fluids enables one to evaluate the occupational hazard to which a worker may be exposed even better than the measuring of the concentration of the compound in air. Some practical examples are given.

Some toxic substances induce changes in blood and urine, such as the appearance or increase of porphyrins, stippled red cells, carbon monoxide hemoglobin, and/or urinary organic sulfates. It is important to know when these changes reach a level indicative of an intoxication. It seems therefore advisable to determine and compare the maximum allowable concentrations of compounds in the atmosphere with blood and urinary findings. This is important, since absorption may occur, in addition, through the skin.

Tolerable Limits in Furfural Intoxication (Research with Rabbits). L. Pecora, N. Castellino, and O. Elmino. Institute of Occupational Medicine of the University of Naples, Italy.

This investigation was designed to establish a threshold limit for furfural using rabbits as the experimental animal. Rabbits were exposed to furfural vapors and dosed repeatedly with liquid furfural by intramuscular injection. Eighty daily intramuscular injections of 200 μg of furfural elicited no clinical evidence of injury in rabbits. The authors regard this as the no-effect level for furfural for the intramuscular route of administration. Eighty daily four-hour exposures to 40-60 ppm of furfural vapor produced no evidence of intoxication in rabbits.

Tolerable Limits and Safe Limits. A. Zambrane. Institute of Industrial Medicine, Naples, Italy.

Tolerable limits are defined as concentrations of industrial chemicals to which workers may be exposed for an unlimited time without clinical evidence of injury. If, however, the exposure occurs under difficult working or environmental conditions and the worker is not in perfect health, there is a possibility that symptoms of occupational disease may arise. Concentrations abso-

lutely free from harmful effects, regardless of the workers' health and the duration of the exposure are called "safe limits" and are always lower than the "tolerable limits."

The concentrations which can be supported without danger to health or the life of the worker depend on the following: (1) absence of illness of any kind; (2) normal working conditions; (3) normal working environment; (4) normal working hours and schedule. If one or more of these is absent, the permissible concentrations should be so low that they are absolutely free from health hazard. This can be obtained by lowering the "tolerable limit" to a "safe limit."

Tolerable Limits in Carbon Monoxide Intoxication (Research with Rabbits). S. Caccuri, L. Pecora, S. Fati, and C. Vecchione. Institute of Occupational Medicine of the University of Naples, Italy.

Recent research in the authors' laboratory has demonstrated that acute and chronic carbon monoxide intoxication produces sideremia and an elevation of urinary protoporphyrins and coproporphyrins. These metabolic manifestations of carbon monoxide intoxication are not accompanied by any clinical evidence of abnormality. On the basis of these investigations the authors recommend that the threshold limit for carbon monoxide be lowered to 50 ppm.

Aspects of Safety Limits in Industry. G. C. E. Burger (G. J. Fortuin, R. Frant, C. A. Boogaerdt and J. H. C. van Mourik). Philip's Health Centre, Eindhoven, and the Laboratory of Occupational Hygiene, University of Amsterdam, Netherlands.

It is highly important that quantitative toxicological data be made easily available to industrial physicians and hygienists.

The list of maximum allowable (acceptable) concentrations presents important data, but, in the author's opinion, represents a not allowable oversimplification of a complicated problem. An example of a list of safety limits (L.S.L.) giving further additional information is presented for consideration, in which a number of important toxicological data are brought together. A similar list would be a very important tool in the hands of the practitioner in the field of occupational health, opening the possibility of a better judgment in practical situations. It would stimulate further research where objective knowledge is lacking and suggest improvement of working conditions, where MAC lists would rather suggest acceptance of expositions to toxic material, when the average MAC value is not surpassed. (Revised from author's summary)

The Maximum Allowable Limits for Biological Data in the Prevention of Industrial Inorganic Lead Intoxication. R. L. Zielhuis. Department of Occupational Medicine, Netherlands Institute for Preventive Medicine, Leiden, Netherlands.

A disturbance of the function of hematopoiesis is seen more frequently and earlier than the occurrence of subjective symptoms or objective signs of intoxication.

The Evaluation of Exposure to Noxious Substances in Industry. R. Frant. Medical Department, Philip's Health Centre, Eindhoven, Netherlands.

A method is given to evaluate the exposition of industrial workers to noxious substances. Not the individual but the exposed group is considered. Individual symptoms are given a certain number of points, and the sum of these points is calculated per 100 employees. By comparing the percentages of the groups on different dates, changes in conditions can be evaluated. With this method the gravity of exposures to a certain toxic substance in different factories or professions can be compared.

Value of Measuring Mercury and Cadmium Concentration in Urine. L. Friberg. Institute of Hygiene, Karolinska Institutet, Stockholm, Sweden.

If urinary values are to have any relevance, variations with time must be carefully considered. It is also necessary, however, to know when the essential exposure occurred. A given concentration of mercury in the urine may in one case reflect contemporary exposure, but in another case it may be attributable to exposure months previously.

That different norms must be used for different salts of the same substance may seem self-evident, but this distinction is not always observed.

Animal experiments have shown that, despite daily exposure to fairly high concentrations of cadmium, almost none is present in the urine during the first postexposure weeks. Excretion begins gradually after a certain degree of damage has occurred, or possibly after a certain threshold value has been reached. The content of cadmium in the urine then increases sharply at the same time as signs of toxicity (proteinuria) appear. Since this increased urinary output of cadmium obviously is by no means expressive of a corresponding increase in the degree of exposure, urinalysis has very limited value as a yardstick for measuring exposure.

Method for the Determination of the Effects of Irritant Gases on the Cilia (Trachea) of Living Animals. T. Dalhamn. Institute of Hygiene, Karolinska Institutet, Stockholm.

For this test, anesthetized rats with exposed tracheas were employed. Ciliary activity stopped within one minute after exposure to 90 ppm of ammonia and 100 ppm of formaldehyde, and after five minutes of exposure to sulfur dioxide. Ciliary activity was followed microscopically.

Contribution to Permissible Concentrations in Occupational Medicine. W. Wulfert. Industrial Hygiene Institute, State Department of Labor, Oslo, Norway.

The author points out that certain MAC's are

accepted internationally while others are used locally. All of these values are based on data which refer to chemically pure compounds, on observations and effects noted in men working in industrial plants, and, finally, on animal experiments. Many questions remain unanswered—for instance, should it be permissible to exceed MAC's as long as the mean daily concentrations do not exceed the maximum allowable concentration.

Little is known about synergism and antagonism of chemical compounds; therefore, it is urged that our knowledge in this field be extended. In the Scandinavian countries, analytical methods to be used have been agreed on. This is most important in order to attain meaningful MAC values.

Comparative Experiments on Lead Concentration in Blood of Animals Kept at Various Levels of Printing Plants. J. K. Teuchmann. Department of Physiology and Labor Hygiene of CIOP, Warsaw, Poland.

Guinea pigs were kept for one year in a lead-"infected" atmosphere and were then subjected to several tests (general behavior, intake of food, changes in growth and weight, roentgenography of the growing bones, and optical, anatomical, and histopathological examinations). On the basis of polarographic and other determinations, it was found that the generally accepted limit of lead in the blood (0.07-0.33 mg%) is definitely too low.

MAC's in the German Democratic Republic. A. Brandt. Institute for Industrial Hygiene, Berlin.

Only recently have MAC values been adopted in the German Democratic Republic. These values will be meaningful and serve a useful purpose if acceptable analytical methods are employed by the various institutes and laboratories. Limits (*Normen*) have been established for 21 chemical compounds, but the individual values were not given.

Importance of MAC Values of Harmful Industrial Compounds and Their Determinations. G. A. Hunold. Institute for Water-, Soil- and Air-Hygiene, Berlin-Dahlem, DBR.

It is important that analytical methods for air are specific and that they require relatively little time. Several determinations should be run during the course of a working day. In some instances, it may be desirable to supplement air analyses by biochemical tests. After exposure to lead, coproporphyrins in urine, and the blood lead content should be determined. These tests are valuable since they give an indication of the total lead absorbed (inhalation, skin absorption and ingestion).

The extent of absorption of chloroform, trichloroethylene, and related compounds is related to the urinary excretion of trichloroacetic acid, while the rate of excretion of sulfobromophthalein by chloroform. Finally, absorption of organic phosphates may be followed by blood cholinesterase activity, and by a certain urine test given in detail in the *Journal of Occupational Health 12:* 37, 1952.

Abstracts

Contribution to MAC's of So-Called "Inert" Substances. H. Drasche. Institute for Occupational Medicine of the University of the Saarland.

Four hundred ten workers were examined who had worked up to 29 years in sinter plants of iron works. In these work areas the average atmospheric particle count was 1500/cu cm, maximal count was 2900/cu cm. Particle size ranged from 0.5 μ to 5.0 μ. Chemical analysis revealed iron oxides to be present from 40% to 45% and free silica from 1.0% to 2.0%. Men who worked in this atmosphere for more than 10 years had bronchitis twice as frequently and sinisitis 10 times more frequently than other workers. Specific fibrogenous effects were not observed.

Relation of the Site of Collection of an Air Sample to Concentration of a Toxic Agent. L. Oppl. Institute of Industrial Hygiene and Occupational Disease, Prague, Czechoslovakia.

The concentration of a compound in the atmospheric air of a workroom is related to the site and to the extent of escape of the material to temperature gradients in the area, and to air currents. It is for this reason that "heavy" compounds are not necessarily found in higher concentrations near the floor. The studies conducted emphasize the importance of providing an adequate exchange of the air in workrooms as well as the proper placement of blowers and suction equipment. The specific gravity of an air pollutant, whether present as a vapor or mist, plays only a secondary role.

Effects of Toxic Compounds on Certain Central Functions. M. Horváth. Institute of Industrial Hygiene and Occupational Diseases, Prague Czechoslovakia.

Concentrations of 400 μg/liter of trichloroethylene (the MAC in Czechoslovakia) produced significant changes in reflex activity in experimental animals, while a concentration of 50-80 μg/liter of CS_2 (the MAC in the U.S.A.) induced changes in the EEG pattern. To determine minimal toxicologic effects, experiments were conducted with rabbits and guinea pigs in which the degree of irritability of the motor cortex was determined after exposure to organic solvents. The author recommends that the neurophysiologic methods used in different laboratories be standardized.

The Requirements of Analytical Methods Associated with Maximum Allowable Concentrations (MAC). Skramovsky. Institute of Inorganic Chemistry, University of Charles, Prague, Czechoslovakia.

Analytical methods used for toxic industrial chemicals have three degrees of precision: *(a)* rapid, exploratory field procedures; *(b)* precise procedures having a sensitivity corresponding to the highest concentration tolerated; *(c)* methods having the highest sensitivity attainable, well

below the limit of the highest concentration tolerated. Methods *(a)* and *(b)* are useful under actual industrial use of chemicals; *(c)* is used in research and in the analysis of biological materials.

The author recommends cooperation on an international scale among laboratories engaged in this type of work. The objective of this cooperative study would be to test methods of analysis and select a number of standard analytical procedures that would be used throughout the world for the analysis of industrial chemicals in the atmosphere and biological fluids. This would culminate in a publication describing the methods, equipment used, and normal values for the constituents. It would be comparable to a pharmacopaeia. The author suggests that this project be undertaken by the Toxicology Commission of the International Union of Chemistry.

Biological Tests for Exposure. J. Teisinger. Institute of Hygiene and Occupational Disease, Prague, Czechoslovakia.

The determination of the atmospheric concentration of an industrial chemical must also be accompanied by information on the amount of chemical absorbed by the worker. The physician is then in a position to evaluate the health hazard associated with the absorption of this quantity of chemical by the complicated "sampling device" — the human body. The author discusses his experiences with a number of biological tests for exposure to industrial chemicals.

Lead—The determination of the concentration of lead in the urine and the blood is a very sensitive test for exposure to lead. There is a considerable variation in what is regarded as a normal range for lead in blood and urine. Most investigators agree that 0.070 mg % is the upper limit of normal for blood lead. The author questions the Soviet report (Lazarew) that clinical plumbism exists with a blood lead level of 0.03 mg %. There is also considerable variation among different investigators regarding the normal range for urinary lead. The upper limit of normal is 0.150 mg/liter which may be associated with evidence of clinical plumbism.

The author states that the MAC for lead in the United States (0.2 mg/m^3) will increase the urine lead level above 0.150 mg/liter and induce intoxication.

A table is presented showing lead excretion following administration of Ca EDTA for diagnostic purposes.

Arsenic—The normal blood arsenic level has been reported to be 0.002 mg %. There is not enough information to make a correlation between normal blood and urinary arsenic levels. Normal urinary arsenic ranges from 0.015 to 0.06 mg/liter (Patty) or 0.0 to 0.100 mg/liter (Taeger and Roth). The author reports a case of arsenic intoxication with a urine level of 4.16 mg/liter which presented no generalized symptoms of intoxication. This is a remarkable case of tolerance to arsenic. The arsenic content of the hair is of little value in industrial evaluation of exposure because of contamination.

Mercury—Normal urinary mercury ranges from 0.010 to 0.020 mg/liter. Grandjean recently reported no correlation between atmospheric mercury exposure and urinary mercury excretion in workers.

Soviet investigators consider American standards for normal urinary mercury levels to be extremely high. They regard a level of 0.010 mg/liter as proof of mercury intoxication in the presence of clinical evidence of mercurialism.

Normal limits for organic mercury depend on the chemical nature of the compound. The author has found several milligrams of phenylmercury compounds in the urine in the complete absence of symptoms.

Cadmium—According to some investigators there is no correlation between exposure to cadmium in the air and urinary excretion. The upper limit of normal is given as 0.020 mg/liter of urine.

Carbon Monoxide—There is no doubt about the value of blood analysis for the detection of carbon monoxide intoxication. A new infrared method appears promising for the analysis of carbon monoxide in expired air. In this method 1 ppm (0.0001 vol %) of carbon monoxide in the expired air corresponds to 0.4% of carbon monoxide hemoglobin in the blood.

Trichlorethylene—Tables are presented showing correlations between atmospheric levels of trichlorethylene and urinary excretion of trichloracetic acid and the clinical significance associated with various concentrations of trichloracetic acid in the urine. Trichlorethanol excretion may also be used as a test for exposure to trichlorethylene. The simultaneous determination of the two metabolites in the urine is recommended as a test for exposure to trichlorethylene by the author.

Benzene—The author recommends the use of urinary phenol as a test for exposure to benzene. Urinary phenol levels exceeding 20 mg/24 hours are regarded as excessive, indicating exposure to benzene; 40 mg/liter is interpreted as exposure to less than 30 ppm of benzene, whereas 100 mg/liter indicates exposure to 30 ppm benzene in the air.

The presence of benzene in the blood or urine simply means that the individual has had contact with benzene. A level of 50 μg per liter of urine indicates slight exposure, whereas 4 mg/liter signifies severe exposure.

The Soviet MAC for benzene is 10 ppm.

Toluene—Urinary benzoic acid is advocated as a test for exposure to toluene. A 24-hour excretion of 2.1 gm of benzoic acid indicates exposure to atmospheric levels below the American MAC for toluene (200 ppm). The Soviet MAC for toluene, 25 ppm, will most certainly not result in benzoic acid excretion exceeding the normal limits.

Aniline—The urinary output of *p*-amino phenol may indicate exposure to aniline, although there is insufficient information to make any definite conclusions. Normal levels of *p*-amino phenol are stated to range from 4 to 10 mg/liter of urine. The author believes that a worker exposed to the American MAC for aniline (5 ppm) would probably have an elevated urinary *p*-amino phenol excretion. The Soviet MAC (less than 1 ppm) would not elevate the urinary excretion of *p*-amino phenol.

Nitrobenzene—The presence of 0.010 mg % of

nitrobenzene in the blood can be readily determined. When the blood level is 0.050 mg %, nitrobenzene can be detected by odor in the expired air. Since *p*-amino phenol is also a metabolite of nitrobenzene, it may be used to detect exposure to nitrobenzene.

Notes on the Concept of Tolerable Limits for Toxic Substances in Industry. J. Roubal. Institute of Labor Hygiene and Occupational Diseases, Prague, Czechoslovakia.

In establishing the tolerable limit for industrial chemicals, each chemical has certain basic characteristics which must be considered. Among the most important are (1) the rapidity with which it produces toxicological effects at a particular concentration; (2) the tendency to accumulate in the body as related to concentrations in the atmosphere; (3) the rate of elimination of the chemical and its metabolites, and (4) the rate of absorption into the body, which depends on physical properties.

In addition to establishing a tolerable limit for chemicals in the air, it would be useful to set also the maximum amount which a worker can absorb into the body during the work day, limits for concentrations, fluctuations in the air, and limits for exposures to these concentrations.

The working environment can be made safe by application of the following general principles: (1) reducing the amount of toxic substance absorbed to limits below the maximum permissible quantity; (2) insuring the purity of the air inspired by local or general exhaust ventilation, wearing face masks if necessary under certain conditions, and (3) as a last resort, introducing intervals free from exposure during the workday, if it is impossible to reduce the amount of exposure by the methods described above. The duration of the intervals would vary with the chemical.

The Importance of Individual Sensitivity in the Evaluation of Tolerable Limits of Toxic Substances in Industry. M. Wassermann, G. Mihail, and G. Bocea. Institute of Hygiene R.P.R., Iassi, Roumania.

Individual sensitivity to toxic substances is a phenomenon which must be taken into consideration in setting tolerable limits for use of chemicals in industry. In presenting the results of animal experimentation with chemicals, in addition to describing the characteristic toxicological responses, the following additional data should be given: (1) the incidence, type and intensity of individual sensitivity as related to species, age, and sex; (2) the concentrations of the toxic substances in air which elicited these reactions, and (3) the maximum concentrations which did not give rise to sensitivity reactions.

Industrial physicians should know about the toxicological properties of a chemical before it is used in industry and before it is sold commercially. Old and new employees should be examined for possible sensitivity to new chemicals and new products to which they may be exposed.

The author states that the Pavlovian conditioned reflex response is the most sensitive method for the detection of deleterious effects caused by toxic substances in air. They cite Smeljansky's work in addition to their own studies to support this view. Clinical experiences of reactions to antibiotics and manganese are also cited as examples of individual sensitivity to industrial chemicals.

Discussion of Methods Employed in the Establishment of MAC Values for New Industrial Compounds. S. Herzog. Institute of Hygiene and Public Health R. P. R., Bucurest, Roumania.

The author discusses and compares MAC values for various solvents in relation to their chemical composition and pharmacodynamic action. The recommendation is made to replace employees as often as possible in those areas where they may suffer exposure to compounds that induce irreversible effects.

Contribution to the Toxicological Evaluation of Industrial Chemicals. B. Barhad and S. Pallade. Institute of Hygiene and Public Health of Roumania, Labor Hygiene Section.

The authors describe the general methods used in conducting toxicological studies in their laboratory in order to establish maximum tolerable limits for industrial chemicals. It is emphasized that laboratory toxicological research requires verification under actual conditions of use in industry. Tolerable limits can be established only after careful statistical and clinical studies have been correlated with the laboratory investigations.

The Toxicological Value of Iron Derivatives of Protoporphyrin in Intoxications With Aromatic Nitro- and Amine Compounds. I. Goldstein and C. Papovici. Institute of Hygiene and Public Health of Roumania, Section on Labor Hygiene.

In summarizing their studies, the authors discuss the value of certain derivatives of protoporphyrin as physiological indicators for establishing tolerable limits of aromatic nitro- and amine compounds. In addition to methemoglobin, sulfhemoglobin is considered particularly sensitive as a test for chronic exposure and early detection of intoxication due to these chemicals. The determination of catalase activity may also be useful.

The Value of Biochemical Tests in Evaluating the Toxicity of Superphosphate. S. Pallade, M. London, A. Roventa and C. Papovici. Institute of Hygiene and Public Health of Roumania, Section on Labor Hygiene.

The toxic action of superphosphate is due to its content of fluoride and its high degree of solubility. Biochemical changes in fluoride intoxication include hypocalcemia, increase in blood inorganic phosphate, inhibition of in vivo alkaline phosphatose and in vitro cholinesterase activity, and increase in urinary fluoride. The concentration of urinary fluoride is recommended as a test for exposure to superphosphates.

Abstracts

The Value of Hematological Changes in Evaluating the Toxicity of Nitrobenzene. M. London, P. Gerban and C. Papovici. Institute of Hygiene and Public Health of Roumania, Section on Labor Hygiene.

The authors found that nitrobenzene and its homologues produce the following hematological changes in experimental animals: (1) hemolysis; (2) reticulocytosis; (3) Heinz body production; (4) increase in methemoglobin and sulfhemoglobin; (5) leucopenia and thrombocytopenia in the peripheral blood; (6) decrease in the maturation index of the erythrocytes; (7) increase in megaloblasts, decrease in the marrow: blood reticulocyte ratio, and diminution in the number of megakaryocytes in the bone marrow.

Recommendations for the Determination of Biological (Maximum) Values (BGK) for Certain Compounds. M. Timar. State Institute of Occupational Health, Budapest, Hungary.

On the basis of his studies, Timar recommends 69 μg% as the maximum permissible concentration for blood lead. For analysis, he recommends the polarographic method of Teisinger, and for the determination of CO-hemoglobin, he suggests Wennesland's method. In his experience, which dealt with exposures up to 26 years in a coking plant, no abnormalities were reported in neurological, otolaryngolical, EKG. and other studies. The concentration of COHb in the blood of these workers did not exceed 10%. The extent of benzene exposure may be determined by the concentration of phenol in urine.

Data Relating to Maximum Allowable or Toxic Concentrations of Carbon Disulfide. L. Magos. State Institute of Occupational Health, Budapest, Hungary.

Results obtained in this laboratory seem to confirm the conclusion based on neurological examinations: Chronic poisoning can be expected to result from five years of exposure to concentrations of as low as 50 mg/M^3.

On the basis of these investigations, it is not known what the maximum allowable concentration should be, except that it must be under 50 mg/M^3. The Institute has proposed to improve the exhaust system and to shorten the working time to six hours daily.

Method for Determining the Influence on Man of Small Doses of Toxic Substances. M. Lukanoff. Institute of Industrial Hygiene and Occupational Diseases, Sofia, Bulgaria.

Using objective methods, it is difficult to detect in man harmful effects of small doses of certain substances. An eye test was used to establish the minimal dose which exerted an effect on the nervous system. The effect becomes evident by a change in optimal frequency. Exciting doses displace the optimum frequency toward higher values, while inhibitions tend to lower it. The method enables one to determine the concentration of compounds encountered in the industrial environment.

Individual Sensibility of the Organism and Physical Labor as Factors in Poisoning with Small Doses of Toxic Substances. F. Kaloyanova. Institute of Industrial Hygiene and Occupational Diseases, Sofia, Bulgaria.

The author carried out experimental animal studies with parathion, investigating particularly the effects on cholinesterase activity and changes in the number of white blood cells. He concluded that chronic effects depend particularly upon dosage level, number of doses, recovery period between doses, and other factors.

Various Methods Used in Establishing the Maximum Allowable Concentrations. E. I. Ljublina. Institute of Industrial Hygiene and Occupational Diseases, Leningrad.

It is certain that the MAC can only be one that induces no harmful effects in men exposed for a long period of time. Only actual experience can prove that a certain MAC was correct. If the given maximum concentration was set too high, then the price paid for such an experience was too high and might have cost a human life. Clinical observations have taught us that the first signs are reflected in effects upon the nervous system. It is usual that nonspecific neurotic symptoms appear before the specific influence of the poison is established. The determination of functional changes of the central nervous system plays a dominant role in the Soviet Union in experimental research leading to the adoption of a certain MAC.

An analysis of unconditioned motor reflexes, e.g. the flexor reflex in rabbits, is currently used by a number of laboratories to determine the threshold concentration of the poison in experiments of short duration. Another method used in determining the effects of a poison on the nervous system is the measuring of a subordination chronaxie of the motor nerve.

The swimming test is one of the integral methods often used. The maximum time of forced swimming is indicative of the performance of an animal whose organism has suffered from a harmful interference, regardless of the particular function which was injured predominantly. The details of this method were presented by Rylova.

In order to determine so-called hidden effects of a poison, it is preferable to place an animal in a subnormal environment. Under such conditions, it is usually possible to determine chronic effects of small doses. By a subnormal environment is meant qualitative and quantitative restriction of food, induced infection of animals, frequent physical exertion, etc.

By the use of pregnant females or young, rapidly-growing animals, it is possible to establish the effects of toxic substances in doses or concentrations which under different conditions could not be determined.

Abstracts

Basic Conceptions for Maximal Allowable Concentrations of Toxic Substances. A. A. Letavet. Institute of Industrial Hygiene and Occupational Diseases, Academy of Medical Science, Moscow.

The term maximal allowable concentration should be used to denote such concentrations of various harmful chemical substances in the form of gases, vapors, and dusts in industrial atmospheres, as, by their constant effect on workers during the work day over a long period of time, can produce no pathological change or disease detectable by means of the presently accepted examining methods.

Naturally, the concentration of a toxic substance in air corresponding to the level of an MAC cannot be regarded as an "optimal" atmosphere. All modern technical facilities should be utilized to achieve lower, preferably zero, concentrations. Under certain conditions, considerably higher concentrations may be permitted as long as the exposure is brief—for instance, exposure to exhaust gases in a garage. Such high values may be allowed if the rest of a work day is not spent in such an atmosphere.

The problem of combined action of various toxic substances is a very complex one and difficult to solve. In this field little scientific information is available. It is difficult, therefore, to evaluate atmospheres containing mixtures of various vapors and gases.

It is beyond doubt that fatigue increases a person's sensitivity to a toxic substance. An elevated environmental temperature as well as physical strain will act similarly.

International cooperation, based on the widest exchange of scientific information, will further the successful development and solution of the problems encountered in dealing with maximal allowable concentrations of toxic substances.

The Evaluation of Present Time Methods and Procedures Used in Different Countries for the Determination and Fixing of Maximum Allowable Concentrations. K. Horiuchi. Osaka City University Medical School, Osaka, Japan.

The author reported on the following data collected during recent years: (1) The upper limit of lead in blood, urine, and feces of normal, healthy Japanese, as well as the lead content in their food and drink; (2) The upper limit and average values of lead in blood, urine, and feces of nonexposed laboratory animals (rabbit, guinea pigs, and mice); (3) Human and animal experiments designed to follow the intake, metabolism, and excretion of lead—*(a)* oral administration of lead acetate to dogs; *(b)* oral, hypodermic, and intratracheal administration of radioisotope lead (Ra D) to guinea pigs; *(c)* oral administration of lead acetate to man, and *(d)* administration and absorption of lead acetate in man by way of the respiratory tract.

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Conference and library facilities of the Medical Center will be available to registrants. Tuition for the course is $300. For further information and applications, write: Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16, N. Y.

Editorials

Accidental Whole Body Irradiation

Persons receiving whole body irradiation with gamma rays and neutrons from a chain reaction develop a fairly predictable clinical syndrome. The usual course of events is a prodromal period of minor symptoms, a period of latency, and then a period of frank sickness called the stage of manifest illness—a term introduced by Thoma and Wald in their article in this issue.

The 31 accident victims whose cases are analyzed by these authors could be separated into five distinct groups. Arranged in ascending order of severity of illness these were: Group I, those who experienced no illness at all, or only the transient nausea and vomiting that characterize the prodromal stage; Group II, those who, after the short latent stage, exhibited a stage of mild manifest illness characterized by blood count derangement and some infection; Group III, those in whom the stage of manifest illness was severe, with clinical complications of hematological damage and some gastrointestinal findings as well; and Group IV, those in whom major gastrointestinal damage was superimposed on bone marrow failure. The illness of the one patient in Group V had a fulminating course from the very onset, in which there was marked nervous system damage.

The best clinical management of an accidental radiation injury case depends in large part upon an early understanding of the degree of damage. The sooner the clinician knows what to expect, the better will be his handling of the problems certain to arise. The practice has been to base the prediction of clinical course mainly upon the dose of radiation absorbed by the victim, but this practice has limitations. In the first place, there are great variations in the way different persons respond to the same dose—variations resulting from differences in basic susceptibility to injury and in the relative state of health at the time of an accident. Secondly, dose estimations must be indirectly calculated from data that usually are a combination of measurements and assumptions and have the further defect of requiring a great deal of time to produce.

Thoma and Wald have developed a new way of accomplishing the all-important, early gradation of case severity. Their method utilizes observable changes in the victim himself. On the basis of generally accepted studies by others, a mean value is given to each component of the blood count. A deviation from this mean is given a score, from 1 to 4, depending on the extent of the deviation. Blood counts are made as soon as practicable after a radiation accident, and are repeated daily. The scores of abnormality are added daily, and thus become cumulative. A cumulative score shows a greater contrast with respect to its mean than does the comparison of any single count with respect to the same mean, with the result that significant abnormalities are shown early. To this simple exercise in arithmetic is added a consideration of the different symptoms experienced by the victim with the passage of time. Applying this method to case records, Thoma and Wald have been able to make severity classifications from the recorded clinical changes in the first two or three days following exposure. The method provides valuable assistance in the clinical management of accidental whole body radiation.

Sickness Absenteeism

The concern of the industrial physician for nonoccupational illness and injury absence has by custom been based upon two considerations. In the first place such absences are indicators of health problems whose solution the industrial physician must help find. Secondly, other things being equal, optimum recovery is facilitated by

an early return to suitable, productive work—an objective achieved with increasing difficulty in these days of complicated labor relations. The traditional concern of management in this problem has been the indirect cost of production loss that accompanies the vacant work station, and the traditional objective of the practicing physician has been to return his patient to work at the earliest possible time to gain for him his needed wages.

The greatly liberalized fringe benefit programs have changed the nature of the nonoccupational sickness absence problem. The problem has suddenly become broader than "sickness." Its solution in a given situation is apt to depend upon an understanding of certain basic attitudes in the total community.

What is the attitude of the workers in this matter? Do they consider it to be their right to be absent a specific number of days each year? Do women workers expect time off during menstrual periods? Do married women feel justified in ascribing time off for home responsibilities, to one or another illness? Or contrariwise, do employees and their representatives resent ineffective workers and those taking advantage of sickness insurance plans? Is it the kind of work force in which one remains at his job and does his best despite minor symptoms of various kinds?

What is management's attitude? Is the manager really interested in the health and morale of his employees in relation to production, or is he indifferent so long as insurance rates are not increased?

And then there is the attitude of the key person in any effort to control absenteeism—the community practitioner who is the employee's personal physician. How does he resolve the frequent conflicts between sound medical judgment and patient-pressure for special consideration?

In his article in this issue, Dr. Robert W. Butler reports on studies made of apparent abuses in two different types of industry in two different states, and describes control measures devised for the second. In this situation, the essential need seemed to be for a removal of the pressures which patients are able to make upon their physicians for loose wordings and actual falsifications of the reports upon which insurance benefits are based.

Book Reviews

WORKING ABROAD: A DISCUSSION OF PSYCHOLOGICAL ATTITUDES AND ADAPTATION IN NEW SITUATIONS. Formulated by the Committee on International Relations, Group for the Advancement of Psychiatry, Report No. 41. Price, $0.50. Pp. 45. New York, The Group, 1958.

In 1956, there were more than 100,000 American civilians working abroad on a full-time basis, of whom 24,000 were engaged in American business enterprises. The figures exclude troops and dependents. These persons moving overseas must adapt themselves in their new environment so as to withstand separation-anxiety, be able to exercise nonjudgemental understanding of the culture in which they find themselves, and, in performing their jobs effectively, find satisfactions and rewards, irrespective of the motivations which led to their move.

This report, one of a penetrating, informative recommendatory series produced by GAP since 1946, has been prepared for the use of psychiatrists and related professional groups concerned with the selection, training, and effectiveness of personnel abroad. Reviewing succinctly are the scope of the problem, the stresses in work outside the United States, the role of the family, personal relationships in the new milieu, and factors in adaptation. The goals and expectations of our citizens abroad vary, and the reactions encountered in foreign cultures may course from overidentification with the local population to complete rejection of the peoples in whose area they live and work, to the establishment of comfortable and communicative relationships with the new groups. Strains can relight old hostilities and prejudices, and the sudden plunge into cultural differences can create psychological difficulties which may negate the worth of the job being attempted, through alienation of the citizens of the foreign country, in whose country the American is the foreigner.

Selection becomes a process of importance, for candidates with psychological illnesses are known to do poorly abroad, and those who are granted waivers, in recognition of states intolerant of stress, have had to return to the United States. Whereas the examination of those considered for this distant duty is of considerable concern to the medical examiners of the Foreign Service of the Department of State, it likewise assumes new dimensions for the physicians reviewing employees for assignment to the overseas business, manufacturing, and distributive activities of American industry. Although success in selection cannot be predicted, the Report does point up the "imponderables" and, through some anecdotal material, factors in adjustment are personalized.

This brochure is recommended not only for those involved in the decisionmaking regarding clearance of applicants, but for any physician who desires a clearer understanding of the interrelationships of

emotional configuration, work stresses, and adaptation. A foreign service training center is suggested, wherein research, evaluation, and consultation could be carried out, and the efforts of those engaged in this activity coordinated in clearing-house fashion. The physicians of companies with interests abroad could lend support to such a proposal, for the benefits which could accrue to the successfully placed worker, the company, and the United States, through bettered relations with other nations, would be immeasurable. A good bibliography is provided, including such items as "The Art of Overseamanship," and "Americans at Work Abroad." Its perusal is earnestly suggested, for in the hands and minds of our representatives abroad lies much of the future of us all—peace and progress, or missiledom and eternal conflct.

—J. S. FELTON, M.D.

CLINICAL EPIDEMIOLOGY. John R. Paul, M.D. Price, $5.00. Pp. 291. The Scientist's Library. Chicago, The University of Chicago Press, 1958.

This book represents Dr. Paul's efforts to interest clinicians in the application of the principles of epidemiology to the daily practice of medicine and consists of his observations and experiences derived from investigations and teaching of clinical epidemiology at Yale University, Department of Preventive Medicine. The distinction is made early that the concept of epidemiology in its proper perspective is concerned with "the circumstances under which diseases occur, where diseases tend to flourish, and where they do not" and goes beyond the study of epidemics.

The presentation is not "statistical" but rather accents the clinical examples of observations on patients, the family, and the community, of epidemiological principles and methods. Although it was emphasized that the concepts developed related to all diseases, the illustrations were predominantly from the infectious group. In Part III, "Sample Diseases," special attention is given to the epidemiology of rheumatic fever, coronary occlusion, poliomyelitis, infectious and serum hepatitis, and arthropod-borne virus infections.

The thread interlaced throughout the various chapters is the physician, the family doctor, and the opportunities for clinical contributions to epidemiology, particularly of the "family" in its broadest sense. The concepts of etiology are conveyed by an agricultural simile of the seed, the soil, and the climate and portray effectively the purpose of the book "to introduce the subject to doctors, or students of medicine, biology or sociology in nontechnical terms."

This is further demonstrated in the three chapters on "Methods and Terms," "Mortality Rates," "Illness Rates and Charting of Data," which provide essential information in a clear, precise, and readable manner. These sections, although continuing to emphasize the clinical approach to epidemiology, make quite clear the necessity for the accuracy of comparable observations through the proper use of "numbers" and "rates."

The two chapters on the environments could be quite stimulating to the clinician, introducing and organizing concepts which have a direct bearing on disease formation. Epidemiological climates are considered as of two types: microclimates or sociologic climates, representing intimate living conditions within the home or place of work; and macroclimates, climate in meteorologic sense, temperature, moisture, rainfall, etc. Climate, altitude, soil conditions, food supply, effect of isolated areas, role of insect vectors, all are considered.

Some recognition is given to occupation and the place of work with case illustrations. However, the intricacies of the epidemiology of occupational diseases with variations of employment data, exposures, in different time periods and population groups, is not included in the text, so that the "general" flavor is carried throughout, although the basic concepts and principles defined certainly apply to all diseases.

The book does bring out the recognition of the general practitioner and the part he may play in preventive medicine, by the incorporation of preventive medicine in his daily practice, through the application of epidemiological principles. The clinician can see better how individual health affects community health, how various factors are interdependent, and how the alteration of one factor may influence the spread or control of a disease. In this manner the effectiveness of the clinician is extended to community health.

—THOMAS F. MANCUSO, M.P.H.

Letters

TO THE EDITOR: I have read the panel discussion entitled "Certification in Occupational Medicine" which appeared in the May, 1959, edition of the JOURNAL, and was somewhat dismayed to find that the American Academy of Occupational Medicine is not mentioned anywhere in this symposium.

In Dr. Kehoe's paper, mention is made of the American Association of Occupational Medicine. If this represents a typographical error and in fact it was the Academy that should have been mentioned, I believe it would be in order to publish a correction. Since it is generally recognized that the American Academy of Occupational Medicine played a significant role in the development of Specialty Certification in Occupational Medicine, it would be most unfortunate if this fact were not given due recognition.

—LEONARD J. GOLDWATER, M.D., President
American Academy of Occupational Medicine

The error was typographical, for which we apologize. We should also like to point out that the trio of articles referred to were intended to explain the qualifications for certification, and the authors made no particular effort to review the developments which led to the establishment of occupational medicine as a specialty. Had this been the case, the American Academy of Occupational Medicine would certainly have been given prominent notice.—Editor

About the Authors

GEORGE E. THOMA, M.D., is senior author of the article in this issue, "The Diagnosis and Management of Accidental Clinical Radiation Injury." His appearance in our new journal brings its own elements of newness. He is the editor of another new periodical, the *Journal of Nuclear Medicine;* he is listed as a practitioner in a new subspecialty of internal medicine called radioisotopology; and the present article by him and DR. NEIL WALD contains impressive new knowledge.

DR. THOMA is the head of his section of the Southwest Medical Center, St. Louis. His hospital appointments in that city include St. Joseph's, St. Mary's Group, Incarnate Word, Missouri Baptist, and Evangelical Deaconess. He is Chief of Medicine at the first of these, St. Joseph's Hospital and he is a senior instructor in medicine at St. Louis University.

In connection with his interest in nuclear medicine, DR. THOMA is consultant to the Health Physics Division of Oak Ridge National Laboratory, to the Medical Division of Oak Ridge Institute of Nuclear Studies, and to Lockheed Aircraft Corporation.

REX H. WILSON, M.D., is senior author of the review article in this issue on "Toxicology of Diisocyanates." He is the author of numerous articles on various phases of medicine, with emphasis upon the clinical and preventive aspects of industrial toxicology problems. These were written from his continuing experience as a practicing internist and as Medical Director of The B. F. Goodrich Company, Akron, Ohio. He is certified both by the American Board of Internal Medicine and in Occupational Medicine by the American Board of Preventive Medicine.

DR. WILSON received his education at Ohio Wesleyan University (B.A., 1931) and at Ohio State University (M.D., 1935). He interned and was a resident physician at Presbyterian Hospital, Chicago. He opened a practice in internal medicine at Akron in 1937 and in the following year began the association with the Goodrich Company that led to his appointment as the firm's Medical Director in 1946.

DR. WILSON was a director of IMA in 1955 to 1957 and is a past president of its Pittsburgh component. In 1948 he was presented the Association's Award for Merit in Authorship as the senior author of an article entitled, "Medical Problems Encountered in the Manufacture of American Made Rubber."

MR. GEORGE L. WILSON is Industrial Hygienist in the Department of Industrial Hygiene and Toxicology of the B. F. Goodrich Company, Akron, Ohio. A native of Indiana, he holds a B.S. degree from Purdue University (Chemistry, 1936). He has been in his present position since 1955. Immediately prior to this affiliation, he was with the West Virginia State Health Department as an industrial hygienist and Director of the Industrial Hygiene Division.

He had overseas duty with the U.S. Army from 1941-1945, holding a rank of Lieutenant Colonel at the close of World War II. He is a member of the American Industrial Hygiene Association and is currently the President-Elect of its Northeast Ohio Section.

MR. WILSON is co-author of the article in this issue entitled "Toxicology of Diisocyanates."

ROBERT W. BUTLER, M.D., reports that since he has seen nothing in print on the subject of abuse of employee sickness insurance plans "except wailing and moaning," he was impelled to write about a plan of control that has proved effective in his hands. The result is his article in this issue, "Group Disability Insurance, Abuse and Control."

Dr. Butler received the A.B. degree from Wesleyan University and the M.D. degree from

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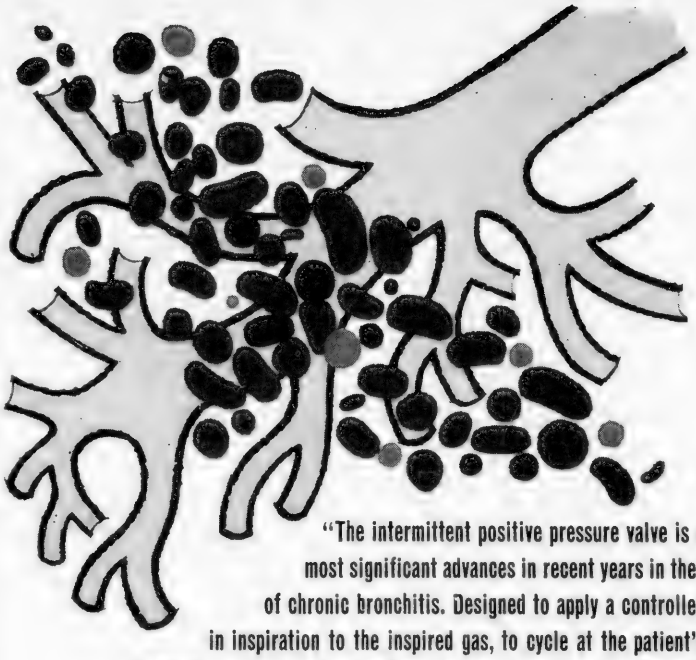
About the Authors

Tufts University School of Medicine. While in private practice at Lawrence, Mass., during the decade 1932-42, he served as part-time plant physician to Arlington Mills.

During World War II, he was a commander in the Navy and industrial medical officer at the Naval Gun Factory at Washington, D.C. After a period of employment as Medical Director, William Whitman Company, Inc., of Lawrence, Mass., he assumed his present duties as Medical Director, Scovill Manufacturing Company, Waterbury, Conn.

Dr. Butler is a participant in several community activities, among them the Cardiac-in-Industry Committee of the Connecticut Heart Association, and is the author of the article "Cardiac in Connecticut Industry," which appeared in the *Connecticut Medical Journal.* He is a Fellow of the Industrial Medical Association.



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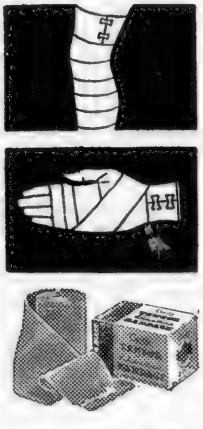

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People and Events

James N. Waggoner, M.D.

John J. Welsh, M.D.

► JAMES N. WAGGONER, M.D., has been named Medical Director of The Garrett Corporation's AiResearch Manufacturing Division in Los Angeles. He succeeds the late A. C. REMINGTON, M.D.

DR. WAGGONER graduated from the University of North Carolina and received his M.D. degree from Indiana University School of Medicine. He is a Naval Air Corps veteran with six years active service, including two years as a flight surgeon aboard an aircraft carrier during the Korean War. He is the recipient of six battle citations.

Following his duty in the Navy, DR. WAGGONER joined United Air Lines in 1952, and for the past two years has been regional Medical Director with offices at Los Angeles International Airport.

DR. WAGGONER was chairman of general arrangements for the 30th annual meeting of the Aerospace Medical Association held in Los Angeles earlier this year, and has served as secretary of the Airlines Medical Directors Association for the last five years. DR. WAGGONER is certified as a Specialist in Aviation Medicine by the American Board of Preventive Medicine.

► JOHN J. WELSH, M.D., has accepted the position of Assistant Medical Director for the New York City offices of the Union Carbide Corporation. He will be associated with JOHN NEILSON, JR., M.D., Medical Director.

DR. WELSH received his bachelor of science degree from Fordham University in 1936 and his M.D. degree from St. Louis University in 1939. He interned at St. Vincent's Hospital, New York City.

From 1941 to 1946, DR. WELSH served with the U.S. Army Air Force as a Flight Surgeon with the rank of lieutenant colonel. After the war, he did postgraduate work at Bellevue Hospital in New York City. He then joined the medical department of American Airlines at Flushing, N.Y., and has been Assistant Medical Director of this organization for the last nine years.

DR. WELSH is a member of the Industrial Medical Association, the Aerospace Medical Association, the Air Line Medical Directors Association, and is certified in Aviation Medicine by the American Board of Preventive Medicine.

► THEODORE L. WILLIAMS, M.D., has assumed the position of University Physician for Indiana University in Bloomington. He was formerly associated with the medical department of General Motors Corporation's Buick-Oldsmobile-Pontiac Assembly Division in Wilmington, Delaware.

DR. WILLIAMS received his M.D. degree from the University of Colorado School of Medicine in 1934 and has done postgraduate work in proctology. He was Health Officer for the city of Denver from 1936 to 1941. He served on the staff at St. Anthony's Hospital in Denver from 1941 to 1944 and then at St. Luke's Hospital, also in Denver, from 1941 to 1950. He was with the medical department of Hanford Engine Works in Richland, Washington, for a while before joining General Motors.

► HAROLD T. LYON, M.D., has been appointed Medical Director of Swift and Company with headquarters in the Chicago general

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People and Events

offices. He will be in charge of all medical departments in the company's organization.

DR. LYON has spent the last 12 years in Harbel, Liberia, as Medical Director for Firestone Plantations Company. He was director of two general hospitals and a clinic providing public health service for 40,000 persons. During this time he was also preceptor of a program of training in medicine in the tropics for senior medical students from the College of Physicians and Surgeons, Columbia University.

Dr. Lyon received his M.D. degree from McGill University, Montreal, in 1936 and interned at the Montreal General Hospital. He was Medical Officer for the British Colonial Medical Service in Nassau from 1937 to 1943, at which time he joined the Royal Canadian Air Force, and served for three years as Lieutenant to Wing Commander, Preventive Disease Section in Canada and England.

► J. R. CHITTUM, M.D., has been appointed Medical Services Manager for the Olin Mathieson Chemical Corporation's Energy Division in Niagara Falls, N.Y.

DR. CHITTUM did undergraduate work at Wooster (Ohio) College and Duke University. He received his M.D. degree from Duke University School of Medicine in 1953, and served a surgical internship and residency at Duke Hospital and the Durham Veteran's Hospital. For the last year DR. CHITTUM has devoted his practice to industrial medicine, serving the Erie Taconite Plant at Hoyt Lakes, Minn.

► JOHN H. FOULGER, M.D., retired July 31 from the position of adviser on toxicology and forensic medicine for E. I. du Pont de Nemours & Co.

DR. FOULGER started with Du Pont in 1935 as senior toxicologist at the Haskell Laboratory for Toxicology and Industrial Medicine, and became director of the laboratory in 1938. Under his direction, the laboratory developed new knowledge and techniques about the hazards of making and handling chemicals and the application of these developments to the safeguarding of users and manufacturers. He was appointed director of medical research in 1952, and was largely responsible for developing Du Pont's extensive research on toxicology.

DR. FOULGER was born in England and attended the University of London, earning a master's degree in physical chemistry in 1922. He came to the United States the following year and attended the University of Cincinnati. He obtained a doctorate in biochemistry in 1924, and an M.D. degree in 1930. From 1925 to 1935 he remained at that university as an instructor in biochemistry and pharmacology.

He is the author of many scientific articles that have appeared in professional journals and is a member of numerous Associations and Societies. He was one of a small group of founders of the American Academy of Occupational Medicine, which was formed in 1946.

► Newly elected officers of the Minnesota Academy of Occupational Medicine and Surgery, who will take office at the September meeting, are: President—JOHN A. WILLIAMS, M.D.; Vice-President—ROBERT GOLTZ, M.D.; Secretary—EARL T. OPSTAD, M.D.; Treasurer—B. A. DVORAK, M.D.; and Recorder—LYMAN B. CLAY, M.D.

Elected to the executive committee are: JOHN SHRONTS, M.D., TRACY E. BARBER, M.D., and C. M. SMITH, M.D.

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► CASSIUS H. WATSON, M.D., retired Medical Director for American Telephone and Telegraph Company and a former president of the American Association of Industrial Physicians and Surgeons, died June 1, at the age of 80, at the Nestledown Convalescent Home in Stamford, Connecticut.

DR. WATSON started his career as a private practitioner in Brooklyn in 1907. Soon the New York Telephone Company began to refer accident cases to him, and as the number of referrals increased, so did DR. WATSON'S interest in industrial medicine. In 1913, the American Telephone and Telegraph Company appointed DR. WATSON medical adviser to its new Employee Benefit Fund plan, and in 1915, he became the company's full time Medical Director.

DR. WATSON was one of the charter members of the American Association of Industrial Physicians and Surgeons which was organized in 1915, and later became the Industrial Medical Association. During the 1920's, DR. WATSON was several times elected a director of the Association and in 1930 he was elected president. Long after his presidential term he continued to participate in the affairs of the Association and contributed much to its growth and progress.

His interest in accident prevention brought him in contact with the National Safety Council. From 1935-1937 he was its president, and for many years afterward served on its executive committee.

DR. WATSON retired from A.T. & T. in 1943 and immediately took over the directorship of Vanderbilt Clinic of the Columbia-Presbyterian Medical Center in New York. He remained there until 1945 when he retired to Brookfield, Conn.

DR. WATSON received his bachelor of science degree from the University of Pennsylvania in 1909 and his M.D. degree from Long Island College of Medicine in 1905. He interned at Long Island College Hospital.

► HARRY EDGAR MOCK, M.D., died at his home in Ormond Beach, Florida on June 30, 1959, at the age 79 years. DR. MOCK was one of the founders of the American Association of Industrial Physicians and Surgeons, the original name of the Industrial Medical Association; and he was the Association's second president. He was in every sense a pioneer of industrial medicine.

DR. MOCK started the examination of employees of Sears, Roebuck and Company in 1909 to discover and isolate the tuberculous. He quickly became convinced of the economic as well as the medical value of thorough examinations and complete case records. Yet these basic procedures, now universally established, remained for many years the source of bitter controversy between management and labor. He also, in those early years, had a vision of the use of a large employee population as serious study material, "a human laboratory," as he verbalized it.

The practice of surgery gradually consumed more and more of DR. MOCK'S time. He had been well educated and trained at Rush Medical College, and at Presbyterian and Cook County hospitals in Chicago. In 1914 he won an appointment as an assistant surgeon on the service of DR. A. S. HALSTEAD at St. Luke's Hospital. He was increasingly in demand as a surgeon and as a surgical consultant, particularly in the treatment of occupational injuries. The subject of skull fracture was for years one of absorbing interest to him, and he worked assiduously at an analysis of published case records of this injury in the literature of the whole world. He rose steadily on the staff of St. Luke's, and served on the faculty of Northwestern University's School of Medicine as an associate professor of surgery.

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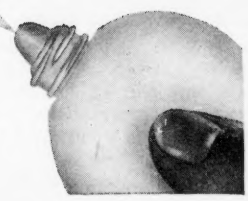

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